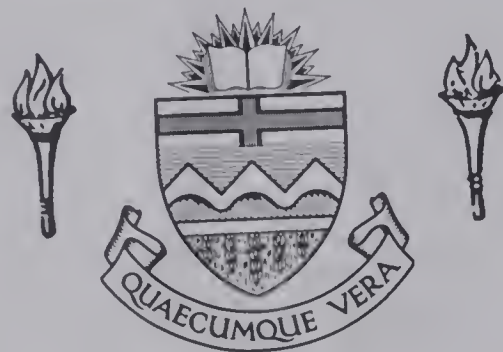


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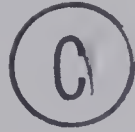
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MANOMETRIC PERFUSION
IN THE MEASUREMENT OF
CORONARY BLOOD FLOW IN THE
DOG. CORONARY RESISTANCE
CHANGES DURING INTRAVENOUS
INFUSION OF ADRENALINE
FOLLOWING LEFT CORONARY
ARTERY OCCLUSIONS.

BY



Richard L. Coulson

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES
IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE
OF MASTER OF SCIENCE

DEPARTMENT OF PHYSIOLOGY

EDMONTON, ALBERTA

SEPTEMBER 1968

THESIS
1968 (F)
40

UNIVERSITY OF ALBERTA
FACULTY OF GRADUATE STUDIES

The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies for acceptance, a thesis entitled Manometric Perfusion in the Measurement of Coronary Blood Flow in the Dog. Coronary Resistance Changes During Intravenous Infusion of Adrenaline Following Left Coronary Artery Occulsion, submitted by Richard L. Coulson in partial fulfillment of the requirements for the degree of Masters of Science.

ABSTRACT

A system is presented which can directly measure flow and peripheral coronary pressure at periodic intervals. A brachial-coronary long-circuit is established, connected by a "T" tube to a pressure transducer and a mercury manometer in parallel. Occlusion of the brachial artery proximal to the "T" tube results in a blood perfusion system for the coronary artery with a head, provided by the mercury manometer. The declining perfusion head in the mercury manometer is monitored by the pressure transducer. The slope of the decline of the perfusion head at the moment of occlusion is directly proportional to the blood flow into the coronary artery when the height-volume relation of the manometer is known. The system can also be used to instantly monitor peripheral coronary pressure (collateral back pressure) by occluding both the brachial artery and the connection to the manometer simultaneously. Records of left coronary artery flow and coronary collateral back pressure in the dog are presented. Calibration is reliable against direct flow measuring systems both in vitro and in vivo.

The system, manometric perfusion, was used to examine the state of myocardial resistance in the vascular bed of the left descending Coronary artery of the dog following ischemic periods produced by temporary occlusion of that

artery.

The system was further used to test the hypothesis: in the dog, ischemia produced by acute coronary occlusion precipitates a change in the adrenergic responsiveness of the coronary vasculature such that the normal coronary dilator effect of intravenously administered adrenaline is reversed to the extent that coronary vascular resistance is actually increased in response to intravenously administered adrenaline.

This thesis maintains that this hypothesis is true, but only to a limited extent. It is submitted that the hypothesis is only completely valid for cases in which the dog heart is rendered partly ischemic by acute permanent coronary occlusion, whereas acute temporary coronary occlusion in dog, can result in such a reversal but does not necessarily do so. It is further maintained that there is no correlation between the duration of such temporary coronary occlusion and the phenomenon of reversed (constrictor) adrenaline responsiveness in the myocardial vasculature of the dog, but that such temporary occlusion can precipitate reversal (constrictor effect).

ACKNOWLEDGEMENTS

I am grateful to Professor John Grayson who so conscientiously supervised, assisted, and guided the work on which this thesis is based.

Thanks are also due to the University of Alberta Central Research Fund and the Medical Research Council of Canada who provided the funds to Professor Grayson which made this work possible.

The technical assistance of Mr. B. Winchester, with the details of I.B.M. APL/360 computer programming, is hereby acknowledged.

The assistance and instruction of Mr. R. Rocher and Mr. T. Villett, who taught me the art of administering anesthetic intravenously is acknowledged.

Finally, but not least, special thanks are due to the staff and students of the Department of Physiology whose help and advice was a constant source of encouragement.

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INTRODUCTION

The classical view of myocardial infarction being the result of an end artery occlusion can no longer be upheld in the light of recent evidence. There is substantial evidence of ample collaterals (7, 16, 24, 27, 29, 31, 37, 38, 48, 60, 61, 62, 63, 67, 74, 84, 106, 116, 131, 141, 188, 189, 197, 209, 236) even in the human heart (14, 132, 162, 163, 177, 194, 198, 217, 234) to sustain an adequate circulation following occlusion of a coronary artery. In order to explain infarction in view of all the evidence of collateral vessels the suggestion of "functional end arteries"

was put forward (248). But, the fact "that the collateral circulation remains patent and potentially effective as a source of blood throughout the infarction process has also been clearly demonstrated (91)" (92). Recently Grayson et al (91, 92, 94, 98) re-investigated the situation, demonstrating that there is a vaso-spastic element in the process of infarction which was found to close off myocardial irrigation gradually, not suddenly as would be the case following occlusion of a simple end artery. More recently, Coulson, Grayson and Irvine (44, 88) have shown that there are at least two orders of functional magnitude describing coronary anastomoses, one arterial (non vaso-active) in nature and the other arteriolar (vaso-active).

In view of the overwhelming body of evidence which has arisen in opposition to the 'end artery' explanation it has become necessary to re-examine the haemodynamic aspects of the coronary circulation. Hence, the present work, which introduces a new technique, that of "manometric perfusion", for the examination of coronary vascular resistance changes in response to intravenous adrenaline infusion.

LITERATURE REVIEW

METHODS OF INVESTIGATING MYOCARDIAL AND CORONARY BLOOD FLOW

The problem of assessing resistance (the quotient of pressure and flow) changes in any vascular bed has always been most acute because of the difficulty in measuring blood flow, the problems associated with obtaining the pressure factor being minor by comparison. Concentration here, therefore, will be applied to the techniques which have been employed to measure flow in various vasculatures, in particular, the heart, since in this organ, probably the most difficulty is encountered. Foremost among the causes of this difficulty are: the superimposition of the heart's own beating on its blood vessels, the

inaccessibility of its arterial origin at the root of the ascending aorta; and, the parallel difficulty of accessibility to the venous termini inside the heart.

It is recognized that all these difficulties can, in part at least, be overcome by techniques which involve the isolated heart (and frequently, the induction of permanent fibrillation). These are all essentially based on the Langendorff (160) perfusion and its myriad subsequent improvements: Heuber and Mancke (126); Uhlmann and Nobile (231); Tripod and Meier (228); Stenikar and Zanolini (224); Stehle (222); Melville and co-workers (178); Lu and Melville (170); Katz and co-workers (145,147); Cameron and Carver (33); Baker (11); Anderson and co-workers (3); Leitch and Haley (165); Truitt (230); Ludena et al (171); Ryser and Willbrandt (204); Larsen (161); Vanremortere and co-workers (164, 235); and Charlier (36). The primary concern here will be with the methods which enable the measurement of coronary blood flow in living mammals with the heart in situ. With this purposeful limitation, this analysis will consist of a grouping of techniques according to the various basic principles with some discussion of their extent and limitations.

1. CANNULATION TECHNIQUES APPLIED TO
THE ANESTHETIZED WHOLE ANIMAL

Cannulation techniques are based on two quite different principles. One is the measurement of blood which flows into the coronary arterial vasculature, and the other is assessment of the coronary venous outflow.

A. Methods for Assessment of Coronary Outflow

Morawitz' Method

Morawitz and Zhan (182) and Meyer (179) simultaneously proposed coronary venous cannulation. Meyer punctured a surface vein while Morawitz cannulated the coronary sinus via an opening made in the right atrial appendix, threading the catheter through the right atrium. This technique is relatively simple and has been used fruitfully by Ginsberg and Scotland (78) and Jourdan maintains the method is an effective screening measure (137, 138, 139, 140, 184).

The main objection to the technique is that it only monitors the portion of the venous outflow which discharges through the coronary sinus. The portion which empties into the cardiac cavities through the anterior cardiac veins and the Thebesian vessels is ignored. This would not be terribly important if the ratio of coronary sinus outflow to total outflow were constant but there is much evidence to indicate the contrary (83, 143, 148, 181, 239). Notably,

Johnson and Wiggers (133) demonstrated wide fluctuation of outflow between the coronary sinus and the Thebesian veins and Graham (83) has shown that the ratio varies from 40 to 80% favoring the Thebesian veins. Thus it cannot be considered realistic to take the coronary sinus outflow as an index of total coronary flow.

Starling's Heart-Lung Preparation

This very commonly used "classical" method includes essentially the same basis as Morawitz' technique, namely, cannulation of the coronary sinus. While being well-known and widely applied and providing much useful data as a coronary flow monitor, it can be vitiated for the same reasons as Morawitz' method. The essentially physiological condition of this preparation is, of course, due to the heart beating under natural conditions, particularly when the cerebral circulation is intact as in Anrep and Segall's (9) modification.

West's Technique

West and co-workers (244, 245) described a technique in which a special cannula is introduced into one of the coronary ostia under fluoroscopic inspection through the carotid artery without, they claim, obstructing coronary flow. The method allows the application of indicator dilution techniques under light anesthesia without major surgery.

The sampling is still made by a catheter in the coronary sinus and is open to the same criticism as above.

Rodbard's Method

Rodbard et al (203) devised a method to measure total coronary venous outflow simultaneously with cardiac output. All blood from the two venae cavae was diverted into a reservoir from where it was pumped through a flowmeter (rotameter) and then into the right pulmonary artery. The coronary venous blood entering the right atrium and right ventricle (95% of total coronary venous outflow) was propelled by the right ventricle into the left pulmonary artery where it was measured by another flowmeter before reaching the lungs. The total of the two measurements yields cardiac output and the second coronary venous outflow. Although the right ventricle is contracting on a reduced mass of blood, the coronary outflow, the general arterial circulation is left intact. This method is a true reflection of the coronary arterial inflow.

B. Methods for Assessment of Coronary Arterial Inflow

These methods, as expected, describe methods of monitoring coronary flow from the arterial side of the circulation.

Melville's Method

Melville et al (178, 170) have described an apparatus highly complex and partly automatic, primarily for use in a Langendorff scheme but it has been used by Lu and co-workers (169) on the heart in situ of the dog. Blood perfusate for the heart from the apparatus is obtained from one of the carotid arteries and is directed into the left anterior descending artery by a dissection and cannulation technique. The main disadvantage would seem to be the inertia of the apparatus which was responsible for a lag between actual phenomena and the recording of it, not a serious difficulty, except that it was an asynchronous lag.

Schofield's Method

Schofield and Walker (210) proposed a technique for artificial perfusion of the coronary arteries so that flow changes independent of arterial pressure could be measured with the heart beating in situ. This method was a refinement of the technique of Dawes, Mott, and Vane (48, 233), Gaddum et al (71) and Burnstein (21) in which perfusion pressure was not independent of systemic arterial pressure. Schofield's scheme was to perfuse the left anterior descending artery with blood pumped through a rotameter by a Dale-Schuster pump. The blood was obtained from a femoral artery and maintained at 37°C. The system was adequate for

assessing mean changes in resistance but the circumflex branch and the right coronary continued to be perfused at systemic arterial pressure while the experimental left descending branch was perfused at the arbitrary rate of the pump asynchronously with the beating of the heart.

Gregg's Method

Gregg and co-workers (110, 112) devised a scheme which allowed the exact measurement of the coronary arterial blood flow under closely approximated physiological conditions (excepting general anesthesia and positive pressure ventilation). Blood from the animal's (dog) own carotid artery provided near normal irrigation of the left coronary artery after being passed through a recording rotameter. A fourth intercostal left thoracotomy was performed. A common carotid artery was attached to the inflow orifice of the rotameter by means of a ligature and the outflow orifice was connected to the left coronary ostium by means of a cannula directed through the origin of the left subclavian artery down the ascending aorta. The cannulae were all secured with ligatures. The original apparatus of Gregg et al (113) used a Shipley-Crittenden rotameter (46, 213). Gregg's method has numerous advantages:

a. the internal cannulation prevents interruption of the coronary circulation and the trauma of dissecting out a coronary artery on the surface of the heart;

- b. the coronary artery received normal blood at normal pressure from the aorta;
- c. the right coronary was irrigated in the normal way;
- d. no pump was needed as the heart behaved normally;
- e. one further important advantage was that Gregg's system also permits the measurement of peripheral coronary pressure and retrograde flow (178).

The rotameter used now has been much improved by Shipley and Wilson (216) but any of a variety of flowmeters could be used instead of a rotameter:

- 1. the bubble-flowmeter as described by Soskin et al (221) and improved by Dumke and Schmidt (57) operates on the principle of an introduced gas bubble (air) being pushed through a special tube by the flowing blood; the bubble is captured prior to the end of the extracorporeal circuit;
- 2. the electromagnetic flowmeter of Denison et al (50) applicable to intact vessels, which is a modification of Richardson's et al (200) electromagnetic flowmeter which was useable only with cannulated vessels;
- 3. Vera's et al (237) drop meter consists of a chamber inserted into the continuity of the extracorporeal circuit; a photocell counter signals a recorder according to the number of drops entering the chamber. Vera claims this device is more accurate than the rotameter.

The extensive use of rotameters speaks for their

accuracy and utility. The bubble flowmeter has been relegated to medical museums. Drop counters have not been widely accepted in spite of their accuracy at low flows. Drop counters have the same attraction as the rotameter; they are direct measuring devices.

Electromagnetic flowmeters, while practical since 1955, have not really come into their own until this decade. They operate on a principle based on Faraday's law of electromagnetic induction, $E = (MLV) \cdot 10^{-8}$, where E is emf in volts; M, the magnetic field in gauss; L, the lumen diameter of the vessel in cm.; and V, the velocity of the liquid in cm/sec. When a conductor, blood, moves through a magnetic field, a voltage is generated in a direction mutually perpendicular to both the magnetic field and the direction of flow. The vessel is held at a constant diameter between the sensing electrodes by a cuff-like probe. The circulation need not be interrupted although originally an electrical-conducting piece of cannula was introduced into the circulation as an extracorporeal link. These flowmeters have several limitations, although they are at present the only practical means of conducting chronic implant experiments:

- a. the electrodes tend to become polarized;
- b. there is induced (quadrature) voltage;
- c. there is unrecorded deviation from symmetrically axial flow distribution;

d. externally generated and physico-chemical artifacts interfere; and

e. flows less than two or three ml/min cannot be measured with any reliability.

Berne's Method

Berne (18) used a method which simultaneously monitored circumflex artery inflow and coronary sinus outflow in dog. An Eckstein cannula (64) was introduced endo-aortically into the left coronary artery. The vascular territory was perfused by a pump with blood from a donor dog. The perfusion pump pressure could be regulated exactly in relation to the recipient animal's aortic pressure. The actual measurements were made with a rotameter.

Manometric Perfusion

This method will be treated in extensive detail as an integral part of the Methods section of this thesis.

2. TECHNIQUES FOR ASSESSING CORONARY BLOOD FLOW IN UNANESTHETIZED WHOLE ANIMALS

A. The Thermostromuhr

The earliest thermostromuhr was that of Rein (199) in 1928. It comprised a small diathermy element and two thermocouples. The diathermy was applied to an intact

blood vessel and part of its heat was cleared by the blood stream producing a temperature difference between the two recording thermocouples. The difference was recorded on a sensitive galvanometer. Baldes and Herrick (12) modified the thermostromuhr by substituting direct current for high frequency alternating current. The method permitted continuous monitoring of mean coronary flow in the subsequently recovered animal. However, Gregg and co-workers (109, 214) pointed out that the results were not reliable because a variety of variables could not be anticipated or controlled. Briefly these were: the extent of stretching of the artery; the position and angulation of instrument relative to the vessel on which it is applied; the presence of back flow in the tissues of close proximity to the instrument; the viscosity of the blood; changes in blood temperature; failure to account for the velocity profile of the blood temperature; and the incorrect assumption that the cross section of blood, at the site of application of the diathermy, was uniformly heated.

B. The Nitrous Oxide Method

Initially this technique was designed for measuring cerebral blood flow by Kety and Schmidt (152) but Eckenhoff et al (59) used it for assessing coronary blood flow in the left ventricle. Fick's principle is the basis of the technique. The blood flow through an organ per unit time

is equal to the amount of (a gas administered) extracted from the blood by the organ in a unit of time, divided by the difference between the concentrations of the gas in the arterial blood and in the total venous blood leaving the organ at the same moment.

In the application of the technique to coronary blood flow measurement arterial blood concentration of nitrous oxide was estimated from blood drawn from any artery and the venous blood concentration was measured in blood sampled from the coronary sinus by catheterization (81, 82). Goodale and co-workers (58, 59) claimed good agreement between results obtained with the nitrous oxide technique and with a flowmeter. No such agreement was found by Gregg et al (108) between results obtained with the nitrous oxide technique and with those obtained with a rotameter. The nitrous oxide method has the advantage of being applicable to unanesthetized animals and even man but it is a periodic measurement, not continuous.

3. HEAT EXCHANGE METHODS

This method of assessing local blood flow in solid organs was first introduced by Gibbs (76) in 1933 and was initially intended for measurement of blood flow in vessels, as was the thermostromuhr. It consisted of a needle-mounted thermocouple which when heated with a constant current recorded a lower temperature in the midst of

high flow than under conditions of low flow. However, this application had all the drawbacks of the thermostromuhr and no more qualifying merit as a flowmeter.

However, in 1952 Grayson (85) demonstrated that heated thermocouples could be used to assess the thermal conductivity of any tissue, or other material, into which they could be inserted. He showed that Carslaw's (34) relation for heat loss from a sphere of infinite mass of material could be applied to results obtained using the heated thermocouple. The relation, $I^2 = F.O.k$: where I = heating current; k is the thermal conductivity; O is the temperature increment produced by the heating current; and F is an instrument constant, was valid provided sufficient tissue or material surrounded the probe.

Kiese and Lange (154) employed heated thermocouples for the measurement of intramyocardial blood flow in animals to effect continuous measurement in 1957. Grayson, who had been using the technique successfully since the early fiftys, with Mendel (95) in 1961, applied the method to the assessment of local flow in the myocardium of rabbits. Since then, Grayson and co-workers (86, 87, 90, 91, 92, 94, 95, 96, 97, 99) have made extensive use of the heated thermocouple method recognizing its significance as a local flow monitoring technique. In spite of Linzell's (168) criticism: ".....results do not confirm Grayson's finding that the cooling of the probe is proportional to

the blood flow except under certain restricted conditions", there can no longer be any serious doubt about the qualitative reliability of heated thermocouple recording of local blood flow in solid organs. It is most useful in measuring distribution of blood flow within a solid tissue (such as the myocardium) and recording changes in distribution following such procedures as coronary occlusion. It does, however, have the drawback of requiring major surgery (thoracotomy) to implant the probes.

4. TECHNIQUES UTILIZING RADIOACTIVE ISOTOPES: THE RADIO-ISOTOPIC TRACER METHOD

The radioactive methods have some unique features, including susceptibility to compartmental analysis (203) and determination by external detectors (42, 43, 5). But, basically they are just variations of the indicator uptake theme like the nitrous oxide technique. There is a number of articles (5, 13, 22, 28, 129, 149, 150, 158, 219) in a volume edited by Bruner (30) which emphasize the use of radio-tracers in peripheral blood flow measurement.

Concerning the coronary circulation in particular, Hansen et al (122) using Kr^{85} found coronary blood flow rates comparable with bubble flowmeter and N_2O results. Conn and Robertson (43) studied K^{42} exchange in the dog heart by maintaining arterial K^{42} constant and analysing the coronary sinus K^{42} concentration curve. This application of the method required cannulation techniques. Conn

(41) has reviewed the external counting methods of assessing myocardial blood flow. The method is very much in vogue at this time but retains many of the difficulties of all variations of indicator dilution techniques and remains only really satisfactory for assessing regional blood flow.

5. SOME NON-QUANTITATIVE TECHNIQUES

Several non-quantitative techniques have been used to assess coronary blood flow. Most have yielded little useful information. Three of these merit attention here. Foremost is the heated thermocouple technique which has been described above:

(A) Lindner's Method

Pituitrin causes vasospasm of the coronary circulation in the unanesthetized animal (10) and increased peripheral resistance causing increased cardiac activity and myocardial hypoxia. Dietrich (51) has found rather exact relationships between the degree of myocardial hypoxia and E.C.G. changes. Lindner and co-workers (167) claim that in a given animal, the E.C.G. changes caused by pituitrin are extremely consistent both qualitatively and quantitatively and that the method used under the exact conditions which they stipulate can be used to evaluate increases in coronary flow. The prime difficulty which presents itself is the

presence of the pituitrin additional to whatever experimental condition is being examined. However, it is the case that the E.C.G. changes can be reproduced in a given animal. The technique is also incapable of accounting for decreases in coronary flow.

(B) Coronary Arteriography

Haight and co-workers (116) demonstrated that increases and decreases in coronary flow could be assessed by angiocinematography. A catheter was introduced into a coronary ostium radiographically by the carotid or subclavian intra-aortic route and radio-opaque material was released outlining the coronary arteries visually by radiology. From the cinematographs, mean diameters of vessels could be measured. West and Guzman (243) have also employed the technique. The method could conceivably be used quantitatively by injecting small amounts of radio-opaque material and measuring its velocity along the vessel and multiplying this value by mean cross-sectional area but it would be clumsy at best.

6. ELECTRONIC AND SONIC METHODS

The electromagnetic flowmeter, which has been discussed above, and the ultrasonic flowmeter are natural developments of an electronic age. The electromagnetic flowmeter holds much promise as has been said already.

(A) The Ultrasonic Flowmeter

This flowmeter (253) takes advantage of the Doppler effect produced when vibrations encounter a moving resistance. The principle of operation derives from the equation:

$$F_1 - F_2 = F_d = \frac{2F_e(V) \cos a}{C}$$

where: F_d = Doppler frequency (instantaneous difference frequency); F_e = frequency of excitation; V = average velocity; a = angle between the acoustical axes and flow; C = velocity of sound in blood.

The method is extremely accurate in the same range in which the electromagnetic flowmeter operates and is much less costly but it has certain important drawbacks. It requires an extracorporeal link to maintain a constant cross-section through which blood can pass (in essence it is a velocity meter). At present, most available ultrasonic flowmeters are not directionally sensitive and cannot account for back flow. This, however, could probably be overcome by phase-sensitive demodulation.

While the entire parade of methods for assessing coronary flow has not been examined, it is hoped an impression has been made of the difficulties encountered in measuring this most critical parameter of physiology.

Since no meaningful analysis of coronary vascular resistance-changes in response to experimental changes of other parameters can be made without obtaining the quotient

of pressure and flow in the heart, the search for a satisfactory blood flowmeter continues. Into the seemingly endless column of attempts will be inserted a refinement of what appeared to be a rather crude technique touched on by Wiggers (250) and Girling (79) and then abandoned without the real significance of the technique being discovered. This technique, designated manometric perfusion by Coulson and Grayson (45), will not be discussed here as it receives exhaustive critique and analysis later in this thesis.

THE ACTION OF EPINEPHRINE ON MYOCARDIAL BLOOD FLOW

Many experimental reports essay description of the sympathicomimetic amine epinephrine (adrenaline) on the coronary circulation.

In general the usual "physiologic" doses and routes of administration have the same qualitative result. This result consists mainly of an increase in systemic arterial pressure and coronary flow. The precise mechanisms responsible for intramyocardial hyper-irrigation are not yet fully understood. It is certain that the result of the stimulating properties of the drug epinephrine (increased pressure head and work of the heart) on cardiac

muscle and arterial vessels contribute to the elevation of coronary flow. It is not, however, so certain that there are direct relaxing effects on the intrinsic resistance of the coronary vessels themselves.

Administered intravenously, epinephrine always increased the coronary flow in the anesthetized intact dog¹. The same effect was observed in the anesthetized dog after close Coronary arterial injection, the coronary flow increasing by an average of 65% for infusions of 9-18 γ /min.².

Two factors responsible for increased intramyocardial flow in response to adrenaline are certain: the increase in aortic blood pressure; and the increased output and work of the heart³. The question, of a direct vasodilator effect operating in the coronary arteries and produced in response to adrenaline is not so clearly defined. There is good evidence, however, favoring such a mechanism in

-
1. Wegria, R., Essex, H.E., Herrick, J.F., and Mann, F.C., The simultaneous action of certain drugs on the blood pressure and on the flow in the right and left coronary arteries. Am. Heart J., 20, 557, 1940.
 2. Driscoll, T.E., and Berne, R.M., Role of potassium in regulation of coronary blood flow. Proc. Soc. Exp. Biol. Med., 96, 505, 1957.
 3. Frank, C.W., Misnahy, G.A., Sioussat, R.S., Sommer, L.M., McCormack, G.H., and Wegria, R. The effect of L-norepinephrine and L-epinephrine on cardiac output and arterial blood pressure in the anesthetized dog. Cited in Bibliography, Wegria, (242).

the intact anesthetized dog:

i. the coronary flow can increase without corresponding elevation of blood pressure and heart rate¹;

ii. measuring changes in peripheral coronary resistance, Wegria et al² proved that there was reduction, whether calculated by the Ohm's law analogy method or by the index (mean coronary flow/mean aortic pressure) on the administration of adrenaline; although it cannot be determined beyond doubt by these experiments it seems reasonable to assume that the coronary arterial resistance fell as a result of a decrease in intrinsic resistance and not as a result of decreased extravascular support.

This opinion is shared by other workers on the entire animal (210)^{3,4} who base their views on the absence of tachycardia and arterial hyper-tension but who could not rule out completely the possibility of alteration in extravascular support, which, however, seemed to them unlikely.

Some relatively recent work has called for

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1. Shipley, R.E., and Kohlstaedt, K.G., Cited in Wegria ibid.
 2. Wegria, R., Essex, H.E., Herrick, J.F., and Mann, F.C., op cit.
 3. Shipley, R.E., and Kohlstaedt, K.G., Cited in Wegria, op cit.
 4. Eckenhoff, J.E., Hafkenschiel, J.H., and Landmesser, C.M., 'The coronary circulation in the dog. Am. J. Physiol., 148, 582, 1947.

re-evaluation of points which had been considered established. Berne (18) has shown that intra-coronary injection of adrenaline in the dog always produced initial reduction of coronary flow followed by a prolonged increase. The reduction in flow was not accompanied by changes in intramyocardial pressure. As the preparation was a constant pressure perfusion of a fibrillating heart, Berne concluded that the initial adrenaline effect was a coronary vasoconstriction.

Wiggers (249) likewise claims that adrenaline increases coronary vascular resistance and that the overall increase in flow is due to stimulation of cardiac force of contraction.

Opposition to the constrictor attitude has been expressed:

- i. by Denison et al¹ who found that intracoronary injection of adrenaline in the anesthetized dog caused a slight reduction of coronary resistance (calculated by direct measurement of peripheral coronary pressure); and
- ii. by Schofield and Walker (210), because in their constant pressure perfusion of the dog heart in situ the increase in flow, at the low dosage level, was not concomitant with changes in heart rate or systemic arterial pressure.

1. Denison, A.B., Bardhanabaedya, S., and Green, H.D., Adrenergic drugs and blockade on coronary arterioles and myocardial contraction. Cir. Research, 4, 653, 1956.

Views on the direction of the effect of adrenaline as a coronary vaso-active substance continue to be antagonistic. "It is, at least, a Pituitrin antagonist" (36)¹.

As the coronary vasodilation produced by adrenaline outlasts the cardiac stimulation, Melville and Mazurkiewicz (178) have suggested that this sustained result may be due to metabolites liberated during the myocardial stimulation.

In most dog preparations including the fibrillating heart (18), the open-chested dog (83), and the unanesthetized dog a few days post-operative to flowmeter implantation² intracoronary artery injection of epinephrine increases coronary blood flow. Intravenous injections increase cardiac oxygen consumption, by increasing coronary flow and decreasing coronary A-V oxygen difference³. With very small doses, coronary inflow may increase without any change in blood pressure or heart rate and with increased coronary A-V oxygen difference. With increased doses, the

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1. Melville, K.I., and Stehle, R.L., The antagonistic action of ephedrine (or adrenaline) upon the coronary constriction produced by pituitary extract and its effect upon blood pressure. J. Pharmacol. and Exp. Therap. 42, 455, 1931, Cited in (36).
 2. Rayford, C.R., A. Huvos, E.M. Khouri, and D.E. Gregg, Some determinants of coronary flow in intact dogs. Physiologist 4 (no. 3):92, 1961.
 3. Feinberg, H., and L.N. Katz, Effect of catecholamines, L-epinephrine and L-norepinephrine on coronary flow and oxygen consumption of the myocardium. Am. J. Physiol. 193:151, 1958.

systemic effects (increased aortic blood pressure, cardiac output, and changing heart rate) intervene and the coronary and metabolic effects are exaggerated (60).

"There is general agreement that epinephrine produces coronary vasodilatation, the flow increase being the net result of an augmented extravascular support tending to decrease coronary flow, a metabolic dilator effect tending to increase coronary flow, and a direct effect which the compound has on the coronary vessels" (106).

Ahlquist's¹ now "classical" paper on adrenotropic receptors has served to elucidate, if not to clarify, the situation concerning adrenaline's action on vasomotor tone. He has proposed that adrenaline's effects, both excitory and inhibitory, can be accounted for by two principle types of receptors termed, for convenience alpha (α) and beta (β): the alpha receptors being responsible for vasoconstrictor activity; and, the beta receptors being responsible for vasodilatation when stimulated by adrenaline. Whether the receptors are actual anatomical-biochemical entities, or simply a verbal shorthand for describing behavior need not be of concern at present since they provide an explanation which is consistent with experimental observations. In any event, it is convenient to speak in terms of increased intrinsic myocardial resistance as a predominance of alpha

1. Ahlquist, R.P., A study of the adrenotropic receptors, Am. J. Physiol. 153, 586-599, 1948.

activity and decreased intrinsic myocardial resistance as a predominance of beta activity when the experimental factor is adrenaline.

The generally accepted view that adrenaline's action on the dog heart is vasodilatory has been voiced in terms of Ahlquist's theory by Parratt (186) who suggested that "adrenaline vasodilatation is due to the dominance of beta (β)-adrenotropic receptors in the myocardial vasculature which mask an effect on alpha (α)-receptors".

Parratt and Grayson (187) in 1966 pointed out that beta blockade reverses the expected dilatory action of adrenaline on the coronary vasculature. In 1968 Grayson et al (92) announced the striking finding that acute coronary ligation of a permanent nature, also reverses the action of adrenaline; "Following coronary occlusion, intravenous adrenaline infusions always produced marked increments in vascular resistance with or without the presence of adrenergic neuron blockade".

It was the object of the present work to determine whether the "adrenaline reversal" found by Grayson and Parratt et al was produced in response to permanent coronary occlusion in acute experiments, as seemed to be the case in their work, or, if the reversal could be invoked by acute coronary occlusion of a transient nature. It was further decided that coronary blood flow would be monitored for this purpose by a method other than heated thermocouple

recording (see Heat Exchange Methods in the Literature Review section of this thesis) to rule out the possibility of a situation peculiar to the presence of heated probes in the myocardium.

To satisfy the demands for a method of assessing volume blood flow into the arterial system of the heart, and also monitoring peripheral coronary pressure, the technique of manometric perfusion was developed.

With a satisfactory method (of assessing volume blood flow into the left descending Coronary artery and concomitantly measuring peripheral coronary pressure) at hand, with the object (of examining myocardial resistance changes in response to intravenous adrenaline infusion following temporary acute coronary occlusion) clear, the present work was undertaken.

METHODS

METHODS IN GENERAL

The over-riding purpose in the exercise was to assess coronary resistance changes in mongrel dogs using the method of "manometric perfusion". This was done by the Ohm's law analogy method of obtaining coronary resistance in the vascular bed of the left descending coronary artery by dividing pressure drop from the ascending aorta to the right atrium by the volume flow of blood entering the left descending coronary artery.

The pressure drop from the ascending aorta to the right atrium was assumed to be equal to the pressure recorded from the aortic arch for the following reasons:

(a) the pressure difference recorded between the ascending aorta and the aortic arch was found to be un-measureable in five dogs (using a cannula introduced through the right internal carotid artery connected to a Statham P-23 pressure transducer recording on a Beckman-Offner, type R.B. oscillograph).

(b) the central venous pressure in the same five dogs was found to be 0 ± 1.2 mm Hg as measured by the same recording system connected to a Statham P-23 pressure transducer with its cannula introduced into the right atrium via the right external jugular vein.

The volume/time flow of blood entering the left descending Coronary artery was assessed by the method of manometric perfusion (45).

METHODS IN DETAIL

1. FLOW MEASUREMENT BY MANOMETRIC PERFUSION

The principle of manometric perfusion (45, 89) was first utilized by Wiggers (250) in 1933 in conjunction with pressure measurement in the coronary vascular bed. It was re-introduced as a crude flow measurement device by Girling (79) in 1951. In neither case was the full potential realized.

The method as utilized in the present instance consists

of the establishment of a brachial-coronary long-circuit, connected by a "T" tube to a pressure transducer and a mercury manometer in parallel. Occlusion of the brachial artery proximal to the "T" tube results in a blood perfusion system for the coronary artery with a head provided by the mercury manometer. The declining perfusion head in the mercury manometer is monitored by the pressure transducer. The slope of the decline of the perfusion head at the moment of occlusion is directly proportional to the blood flow into the left descending coronary artery at the instant of clamping. The relationship is governed partly by the height-volume relation of the manometer and partly by the difference between the aortic end (static side) pressure and the brachial by-pass "T" tube (dynamic side) pressure.

The system can also be used to sample directly peripheral coronary pressure (176) (collateral back pressure).

The present application of the method was developed for use with a long-circuit technique involving the left descending coronary artery. For the purpose of these experiments it was necessary to measure flows which ranged from zero to sixty ml/min. Many of the standard methods are disappointing at low levels of flow. Manometric perfusion has the advantage of simplicity, but more important, it was found to be accurate at any level of flow, from one hundred twenty-five ml/min. to zero.

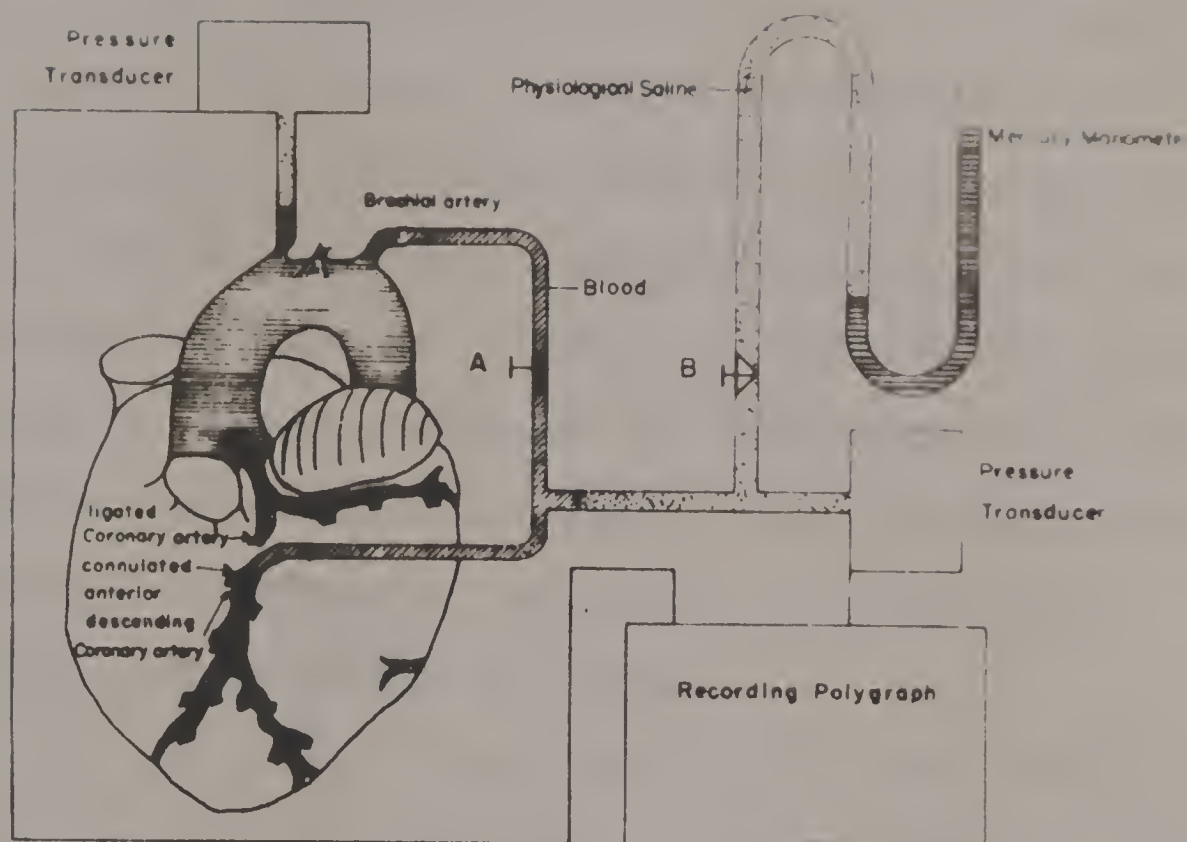



Fig. M-1

Principles of manometric perfusion. Clamping at A - mercury manometer becomes perfusion head. Pressure monitored by transducer. Clamping at A and B, transducer monitors peripheral coronary pressure.

Fig. M-1 illustrates the principles.

A long circuit was established from the left brachial artery of the dog (anesthetic - sodium pentobarbital 30 mg/kg) to the anterior descending branch of the left coronary artery (left descendens). Intramedic  P.E. 240 polyethylene tubing was used and the system included a side arm which led into a mercury manometer and a Statham P-23 pressure transducer connected in parallel. The transducer monitored pressure in the mercury manometer recording on a Beckman-Offner type R.B. oscillograph.

With both valves (see Fig. M-1) A and B open, blood flowed along the long circuit from brachial artery to left descendens. Perfusion pressure for the maintenance of coronary blood flow was the systemic arterial pressure monitored by a second transducer connected by a cannula (directed through the right internal carotid artery) to the ascending aorta.

On closure of valve A, the coronary vessel was cut off from direct connection with the systemic circulation except through collaterals. The perfusion head became the mercury manometer. As pressure declined in the mercury manometer blood was driven from the side tube into the perfusion area; i.e. the vascular bed of the left descendens. The rate of pressure decline will be shown to provide a direct measure of flow. This rate of decline was monitored by the transducer coupled in parallel (Fig. M-2 and M-5). The

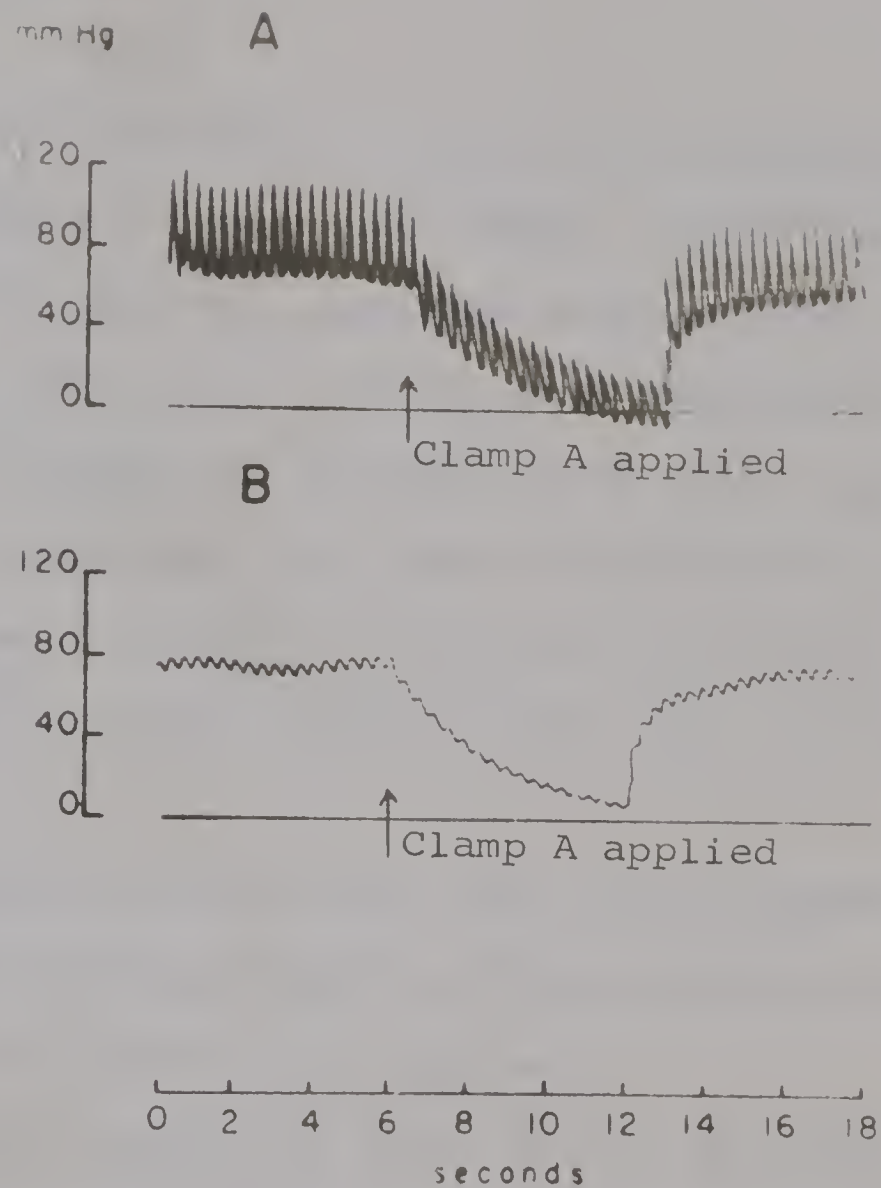


Fig. M-2

Pressure decline when clamp A (fig.M-1) is clamped.

- A. Undamped pressure record. The pulsations after clamping are generated by the direct action of the heart on the occluded coronary vessels.
- B. Mean pressure changes on clamping at A (fig.M-1). Pulsations damped electronically.

In actual flow measurement pressure is not allowed to fall as much as here. This record is presented to illustrate exponential nature of 'die-away'.

interpretation of the pressure decline in terms of flow will now be considered.

A. Flow Pressure Relations in Rigid Tube Perfusion Systems

Fig. M-3 shows a rigid tube system. When free flow was permitted, pressure P_1 , declined non-linearly as fluid left the system (Fig. M-4). It is clear that since the vertical tube, in which P_1 is measured is both a perfusion reservoir and a manometer, the rate of decline at any moment of time is a simple function of flow at that moment.

The immediate problem concerns the exact mathematical relationships.

The appearance of the curves (Fig. M-4) suggests an exponential relationship between pressure decline and time. The following is a theoretical approach -

$$\text{Flow in such a system is given by } F = (P_1 - P_2)/R \quad ((1))$$

The volume of fluid that flows during a pressure decline, dP_1 is given by:

$$F = dV/dt = K_1 \cdot A \cdot dP_1/dt \quad (\text{where } K_1 \text{ is a constant}) \quad ((2))$$

and A is the cross sectional area of the manometer tube), since pressure can only drop by fluid flowing from the manometer.

From ((1)) and ((2)), then:

$$F = (P_1 - P_2)/R = -K_1 \cdot A \cdot dP_1/dt \quad ((3))$$

Let P_t be the effective perfusion pressure at time t , i.e. $(P_1 - P_2)$.

Therefore: $-dt/K_1.A.R = dP_t/P_t$ ((4))

Integrating: $\ln P_t = -t/K_1.A.R + K_2$ (where K_2 is an integration constant) ((5))

so that: $P_t = e^{(K_2 - tK_1.A.R)}$ ((6))

At time zero, $P_0 = e^{K_2}$ (where P_0 is the initial perfusion pressure) ((7))

Differentiating ((6)) with respect to time gives:

$$dP/dt = (-P_0/K_1.A.R) e^{-t/K_1.A.R} \quad ((8))$$

When pressure is measured in mm Hg, time in seconds, area in mm^2 , flow in $\text{mm}^3/\text{sec.}$, then $K_1 = 1$, since from equation ((2)) $F = dV/dt = K_1.A \cdot dP/dt$. Rearrangement of terms gives: $K_1 = 1/A \times F/dP/dt$ and since,

F is in $\text{mm}^3/\text{sec.}$

A is in mm^2

$\frac{dP}{dt}$ is in mm (Hg)/sec.

then $K_1 = \text{mm}^3/\text{sec}/\text{mm}^2 \times \text{mm}/\text{sec} = 1$

To convert flow in $\text{mm}^3/\text{sec.}$ to $\text{cm}^3/\text{min.}$, the flow in $\text{mm}^3/\text{sec.}$ is multiplied by a factor of 0.06.

Under these conditions:

$$F = (0.06 P_0/R) e^{-t/A.R} \quad ((9))$$

From actual pressure-time records, the equation

((6)) with $K_1 = 1$ was fitted by the method of least squares to obtain the decay time constant $A.R. = \lambda$.

The flow at time $t = 0$ is then given by: $0.06 A.P_0/\lambda$.

Measurements of A in the manometer used in this work gave a value of 3.83 mm^2 so that $0.06 A = 0.53$.

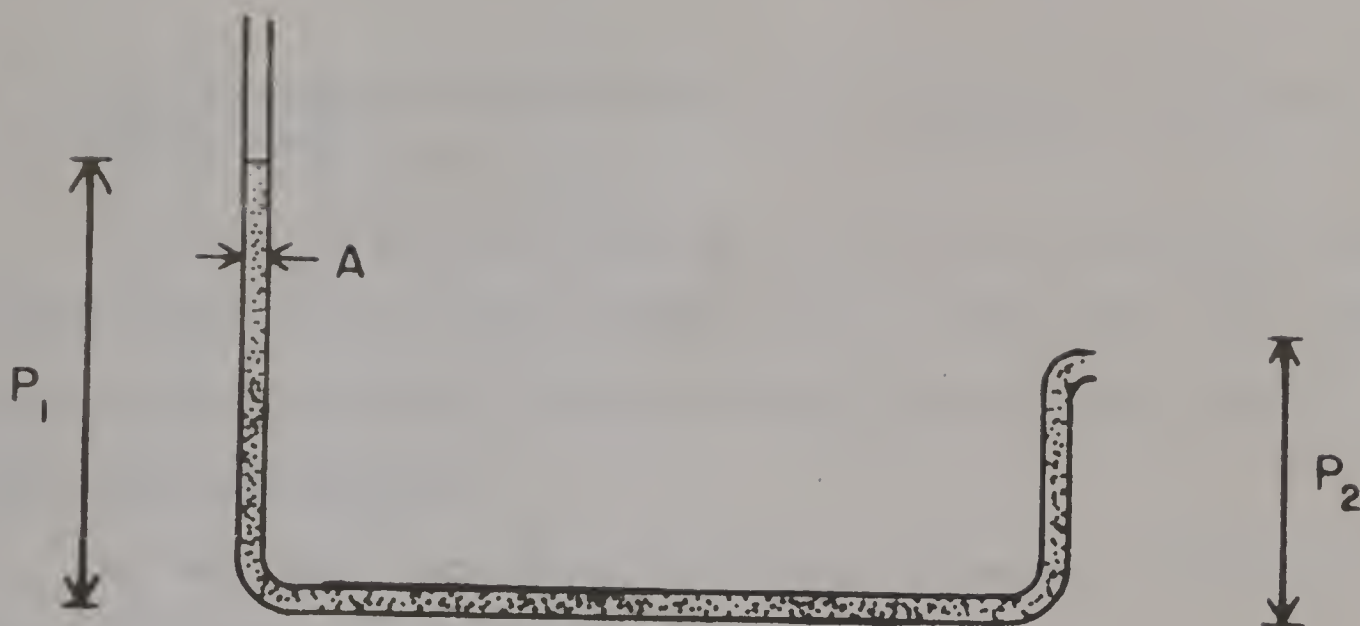


Fig. M-3

Rigid tube system to illustrate haemodynamic basis of manometric perfusion. $P_1 - P_2$ = perfusion pressure. A is cross sectional area.

This figure, 0.53, was designated the 'manometer constant' and it must be determined for every manometer which is used for manometric perfusion flow measurement.

B. Flow-Pressure Relationships for In Vivo Long Circuit Experiments

P_1 was the pressure in the manometric perfusion apparatus manometer when valves A and B (see Fig. M-1) were open under conditions of flow from the brachial artery into the left descendens.

P_2 was the peripheral coronary pressure recorded when valves A and B were closed.

Fig. M-2 shows the curve of pressure decline which followed clamping of the brachial artery (valve A in Fig. M-1). In this experiment the pressure was allowed to die away to a base line which was the pressure transmitted across the collateral network mainly from the circumflex artery.

This curve and all others similar fitted well the treatment described above for rigid tubes and the same mathematical approach is valid. (See Appendix I.)

C. Determination of Flow From Die-Away Curves

In the first experiments flow was determined by drawing tangents to the curve at its origin and measuring directly the rate of fall.

This simple approach, however, was liable to subjective

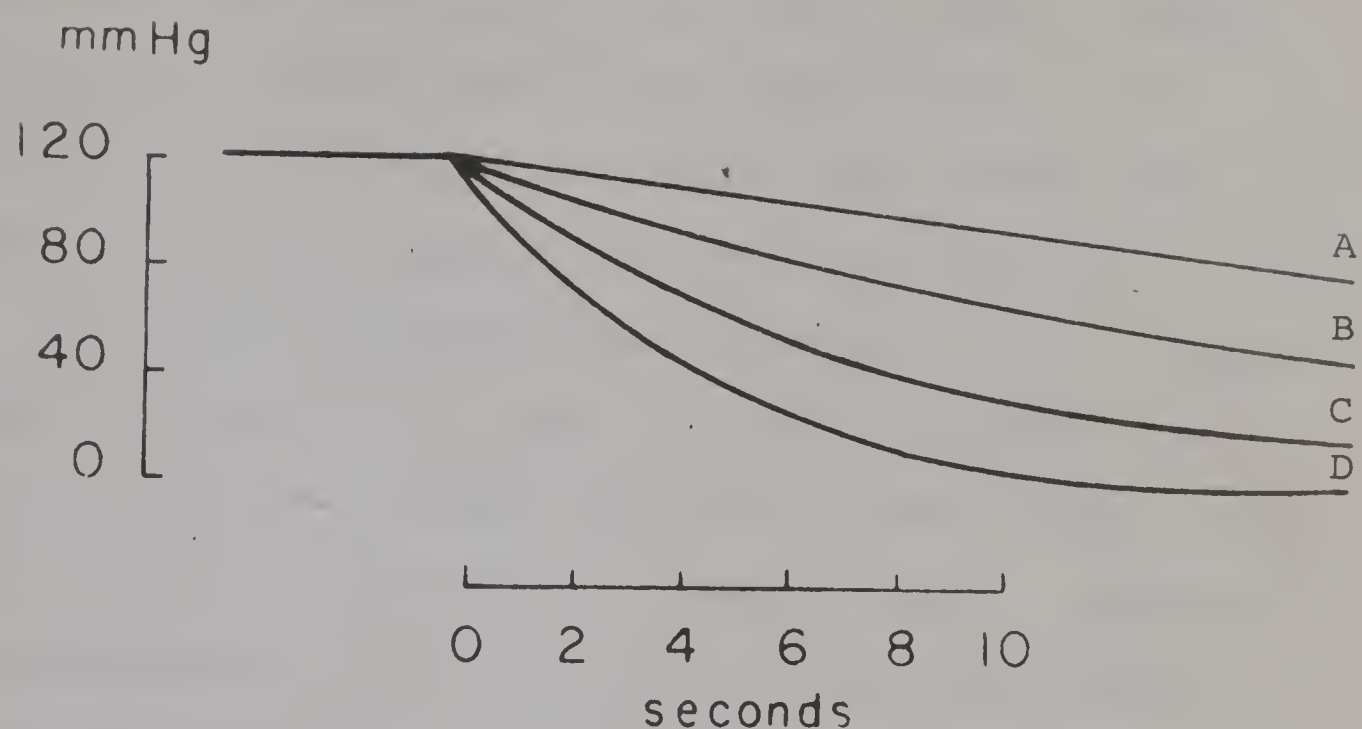


Fig. M-4

'Die away' curves at different flow rates. Initial pressure = 120 mm Hg. in polyethylene tube perfusion system. A = 3.82 ml/min., B = 7.6 ml/min., C = 15.3 ml/min., D = 38.2 ml/min.

error, especially when the 'die-away' was rapid.

Since the 'die-away' is exponential and its mathematical relationships are known it is possible to calculate the slope at time zero from a small number of pressure samples made during the decline. Measurement of such pressures can be made without the subjective errors implicit in drawing tangents.

In routine operation for flow measurement, four sample pressures were taken from the manometer record during the pressure decline at times 0 sec., 0.5 sec., 1.0 sec., and 1.5 sec. (Fig. M-5A). Systemic and peripheral coronary pressures were also sampled to define the limits of the exponential decline. The other four points were enough to calculate the slope of the curve at systemic pressure. The measurement of peripheral coronary pressure was, in routine operation, only made at five minute intervals to eliminate any artefact influencing flow measurement due to reactive hyperaemia. The extent of occlusions used in flow measurements were found to have no effect that could be recognized as reactive hyperaemic responses. However, the occlusions used in peripheral coronary pressure measurement, in the present work, were total but of brief duration (not more than 2 seconds) and did have some slight effect of precipitating a short lived reactive hyperaemia.

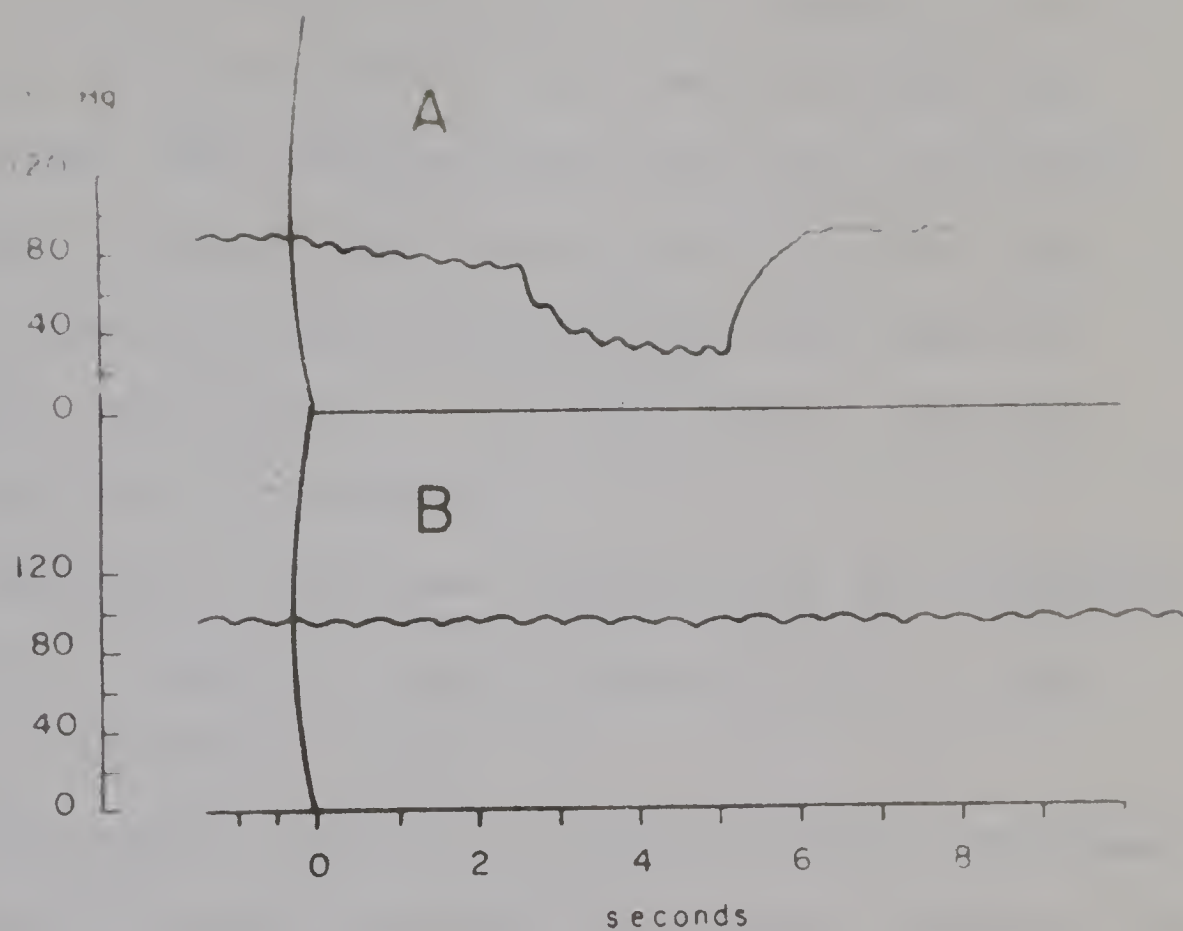


Fig. M-5

Actual flow record as used for flow and peripheral coronary pressure measurement.

- A. Flow record. Initial, shallow slope - result of clamping at A (fig. 1). Pressures measured at 0, 0.5, 1.0, 1.5 secs. Second portion of this curve peripheral coronary pressure measured by clamping at A and at B (fig. 1). Measured at time 5 secs.
- B. Mean systemic pressure recorded through readings. Sampled at time 0.

This reactive hyperaemic response was very slight and disappeared in less than one minute but nevertheless peripheral coronary pressure measurements were normally made only every five minutes or so and the flow measurements made between them were calculated from interpolated values for peripheral coronary pressure which were arrived at from the actual periodic measurements which were made by totally, but briefly, (not more than 2 seconds), occluding the circulation.

Appendix I provides justification for accepting only four samples as being representative of the entire 'die-away' curves.

The actual pressure in the manometric perfusion manometer during conditions of brachial-coronary flow was less than systemic static pressure, by a factor which is a function of the velocity of flow past the side arm. However the constant of exponential decline, and, hence, vascular resistance did not change during any single measurement. (See Appendix I.) Flow at true systemic pressure is therefore given by:

$$(P_A - P_2/P_1 - P_2) \times F$$

when P_A = static pressure, P_2 = peripheral coronary pressure, F = flow corresponding to $(P_1 - P_2)$. This correction is only important at high rates of flow.

While the calculations are simple and direct they are, in fact, lengthy. To facilitate the calculation of flows from the many sets of samples which are taken during the course of any one experiment a computer program has been written using the machine-executable version of the Iverson language¹ known as APL. (See Appendix II.)

Since pressure and flow were both available in the computation, the program was expanded to include calculations of total vascular resistance (pressure \div flow), resistance from aortic to peripheral coronary pressure ((aortic pressure - p.c.p.) \div flow), and resistance from peripheral coronary level to the venous side (p.c.p. \div flow), and a statement of the square of the correlation coefficient relating the curve determined from the four time samples to the ideal exponential curve of the form $P_t = P_0 \cdot e^{-at}$: where P_t = pressure at time t ; P_0 = initial pressure; t = time; and $-a$ = constant of exponential decay. (For a justification of the assumption that the manometric perfusion pressure decline is exponential see Appendix I.)

Following are some examples of the method in use.

1. Iverson, K.E., A Programming Language; John Wiley, New York, 1960.

TABLE M-1

CALIBRATION DATA DERIVED FROM RESERVOIR PERFUSION OF
A FIBRILLATING DOG HEART AS SUPPLIED TO THE COMPUTER

Peripheral Coronary Pressure (mm Hg)	Systemic Perfusion Pressure (mm Hg)	Sample No. 1 (mm Hg)	Sample No. 2 (mm Hg)	Sample No. 3 (mm Hg)	Sample No. 4 (mm Hg)
13	129	83	61	50	43
15	61	53	44	37	34
12	42	40	35	31	29
8	33	32	29	27	25
9	25	25	24	23	22
10	33	32	29	27	26
14	42	39	34	31	29
15	65	56	45	40	36
20	131	90	69	58	51

TABLE M-2

TABLE M-2A CALIBRATION. COMPUTER CALCULATIONS FROM TABLE 1
TABLE M-2B DIRECT FLOW MEASUREMENTS

TABLE A COMPUTER CALCULATIONS				TABLE B DIRECT FLOW MEASUREMENTS	
Peripheral Coronary Pressure (mm Hg)	Systemic Perfusion Pressure (mm Hg)	Left Flow (ml/min.)	Resistance (Newt.sec.cm ⁻⁵)	Cor. Coef. Squared (R ²)	Actual Flow From Reservoir (ml/min.)
13.000	129.000	38.320	3.000	0.982	38.200
15.000	61.000	15.230	4.200	0.983	15.300
12.000	42.000	7.520	6.200	0.985	7.640
8.000	33.000	3.970	8.700	0.997	3.820
9.000	25.000	1.830	17.100	0.999	1.910
10.000	33.000	3.730	10.100	0.968	3.820
14.000	42.000	7.550	6.700	0.983	7.640
15.000	65.000	15.090	4.500	0.978	15.300
20.000	131.000	37.460	3.300	0.984	38.200

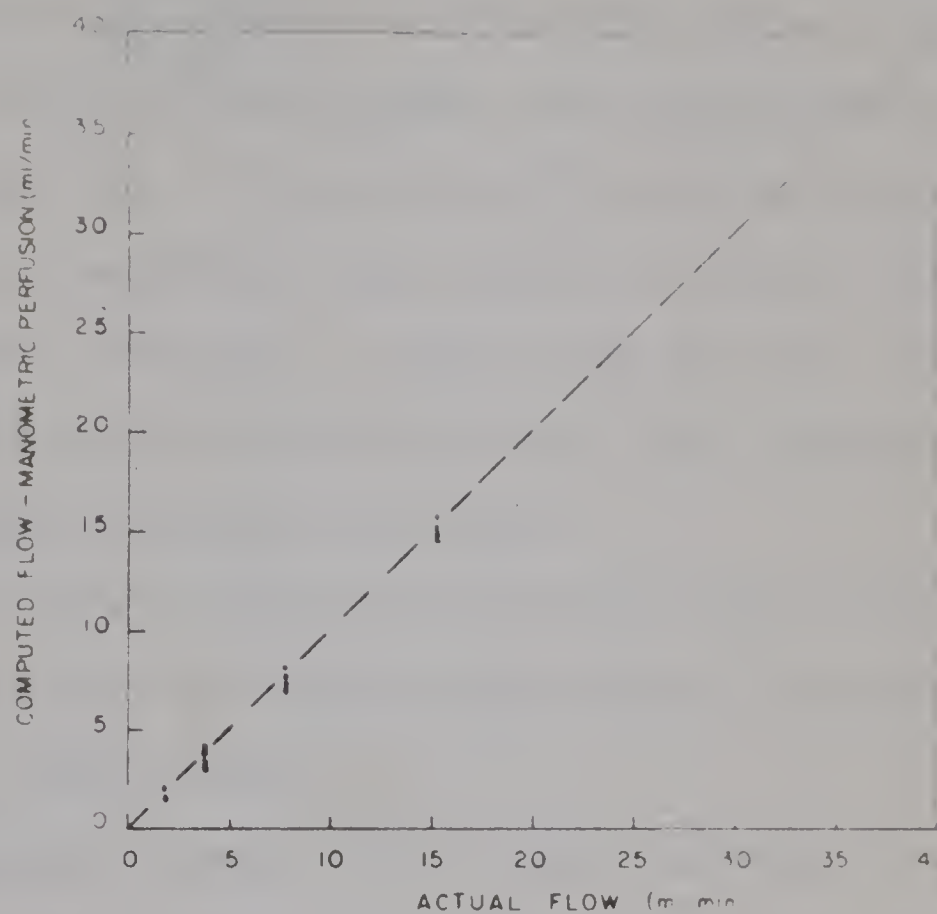


Fig. M-6

Calibration curve. Direct flow measurement from coronary perfusion of fibrillating hearts, estimated flow - computer output.

Table M-1 is a list of sample sets, as presented to the APL program, taken under controlled conditions when the flow was known and provided artificially from a graduated reservoir to the left descendens of a fibrillating heart.

Table M-2A was the resulting flow and resistance measured by the manometric perfusion technique and displayed in the computer off-print. Table M-2B was the actual flow from the artificial source reservoir. All pressures are integrated mean pressures in mm Hg.

Fig. M-6 is a composite curve from three similar calibration experiments of fibrillating hearts (including the data given in Table M-2).

The apparatus used in the present work has a range of 0 to 125 ml/min. At high flows the error was negligible. Even in low range of flow the maximum error recorded was only 4.1% i.e. 0.064% of full scale.

All sample sets were taken at 1 minute intervals but it is quite feasible to take a sample set every five seconds.

2.

ANESTHETIC

General

The anesthetic used in all these experiments was

Nembutal (Sodium-Pentobarbital)¹. The initial product was veterinary grade sterile solution 60 mg/ml in ethanol. For purposes of administration it was further diluted with physiological saline of standard mammalian Ringer concentration.

A. Dosage

The initial dosage used was 30 mg/ml injectate/kg body weight of animal intravenously or 40 mg/ml injectate/kg body weight intra-peritoneally. Maintenance dose was approximately 30 mg/ml injection per animal per hour thereafter but this varied slightly from animal to animal depending on individual response to the anesthetic.

B. Administration

Anesthetic was administered initially by trans-cutaneous puncture of the left or right Cephalic or Median anti-brachial veins depending on accessibility in individual dogs. In the occasional unco-operative animal (four cases) the initial dose was administered intra-peritoneally. Maintenance dosage of anesthetic was administered through a cannula in the left femoral vein. The femoral venous cannula was installed through a cut-down incision in the

1. Nembutal -- veterinary sterile solution, Pentobarbital Sodium. U.S.P. 60 mg/ml in 10% Alcohol, 20% Propylene Glycol U.S.P. and 70% sterile water; pH adjusted with Sodium Hydroxide; Product of Abbott Laboratories.

region of the femoral triangle.

Number 20 G I Yale disposable needles were used in conjunction with 10 ml. Leur Loking syringes for all initial injections of anesthetic. Maintenance doses administered via the left femoral venous cannula were delivered by a similar 10 ml. syringe.

C. Responses

All animals but four responded to the initial intravenous dose with deep anesthesia. Of the four exceptions, one died immediately and three required further injections. One of these required three times the expected dose in order to obtain a suitable major surgical anesthesia level.

D. Comment

Some question has arisen recently concerning the pertinence of cardiovascular observations made during acute experiments performed using barbiturate anesthetics. While there is no denying the fact that Nembutal is a potent vasodilator, observations made during these experiments suggest convincingly that the effect is only transient in nature never lasting more than a few minutes. To the other arguments voiced against Nembutal some consideration must, however, be given. Olmstead and Page (185) have summed up the objections in a recent paper which confirms that there is substantial increase in dog heart rate with

Nembutal used as an anesthetic. They point out also, that this is counter-balanced by a corresponding decrease in stroke volume such that cardiac output is not significantly affected.

3. SURGERY

General

As indicated previously, aseptic technique was not employed in these experiments as all were acute exercises not exceeding six hours duration. No animals were permitted to recover from anesthesia. In all cases, the regulations governing animal experimentation, as set out by the "Committee on Animal Care" under the auspices of the Canadian Federation of Biological Societies, were strictly adhered to. Haemostasis was by a combination of ligatures and electrocautery.

A. Preparation

The anesthetized animal (dog) was fastened in supine position with the limbs secured, outstretched. The left Femoral vein was cannulated by venous cut-down in the region of the left femoral triangle. At the same time the

left Femoral artery was dissected out and a pair of ligatures passed around it for possible later use as a source from which to induce death by hemorrhage. A tracheotomy was performed. The trachea was cannulated with a glass "T" tube for later application of positive pressure ventilation. The right common Carotid artery was dissected out of the neck through the tracheotomy incision and two loose ligatures were passed around it for later use in directing a cannula into the Aortic arch. The left Brachial artery was dissected out of the anterior compartment of the left forelimb from the anteromedial aspect and two loose ligatures were passed around it for later attachment of the manometric perfusion apparatus. The thorax was opened at the level of the fifth intercostal space and positive pressure ventilation through the tracheal cannula was commenced (using a Harvard small animal respirator pump). The animals were then Heparinized¹ with 400 I.U./kg body weight to prevent coagulation in the various cannulae.

B. Establishment of the Manometric Perfusion Long-Circuit

Fig. M-1 illustrates the principles.

i. The previously dissected Carotid artery was cannulated and connected to a Statham P-23 pressure transducer

1. Heparin Sodium, U.S.P., 151 units per mgm. Lot - 101-2, Connaught Medical Research Laboratories, Toronto, Ontario, Canada.

recording on a Beckman-Offner, type R.B. oscillograph. The cannula was pushed retrogradely through the Carotid artery until the distal tip came to lie in the arch of the Aorta.

ii. The polyethylene line from the manometric perfusion apparatus was used to cannulate the previously dissected Brachial artery, also in a retrograde dissection.

iii. The catheter leading from the side arm of the "T" tube in the polyethylene line from the manometric perfusion apparatus was introduced into the left chest through a probe-puncture hole in the antrolateral aspect of the third intercostal space lateral to the left internal Mammary artery. The catheter was then threaded through the chest and brought out through the thoracotomy incision.

iv. The lower lobe of the left lung was packed down with warm saline-moistened cotton wool.

v. The pericardium was incised for a distance of about 50 mm parallel but about 10 mm anterior to the left Frenic nerve. The cut edges of the pericardium were fastened to the edges of the thoracotomy by four pairs of Spencer-Wells forceps at the corners of an 80 mm square "operative window" bringing the left ventricle close to the chest wall.

vi. The anterior descending branch of the left Coronary artery (left descendens) was dissected clean for a distance of about 5 mm as high up the wall of the left ventricle as was possible without interfering with the action of the left

atrial appendix. Two loose ligatures were passed around it.

vii. The dissected portion of the left descendens was ligated and cannulated distal to the ligature with the catheter leading from the side arm of the manometric perfusion apparatus. Coronary left descendens flow was resumed, supplied from the left Brachial artery (through the manometric perfusion long circuit) after periods of occlusion which varied from 1.5 minutes to 36 minutes depending on the experiment.

viii. The manometric perfusion long-circuit established, the packing on the lower lobe of the left lung was removed, the cut edges of the pericardium released, and the thoracotomy was closed with Spencer-Wells forceps.

This surgical procedure resulted in a relatively intact coronary circulation preparation, though including about 150 mm of extra-corporeal circuit from Brachial artery to left anterior descending Coronary artery with a right angle turn through the "T" tube in the apparatus. The preparation was then suitable for control or experimental maneuvers.

4. EXPERIMENTAL AND CONTROL EXERCISES

General

A total of sixty-nine experimental and control infusions of adrenaline or saline were carried out on a total

of 28 mongrel dogs (Table M-3 lists the weight, age, sex, occlusion duration, and number of infusions, whether experimental or control.) prepared as described above. Of these, 24 control infusions of physiological saline solution were administered to 7 dogs and 45 experimental infusions of adrenaline solution were administered to 21 dogs.

5. CONTROL (SALINE) INFUSIONS

General

Saline for control exercises was administered intravenously at the rate of 0.68 ml/min from a 50 ml syringe by a Palmer infusion pump through the cannula in the left Femoral vein.

A. Pre-Infusion Considerations

Having established the manometric perfusion long-circuit, a reasonable number of measurements were made using the apparatus to determine: peripheral coronary pressure; aortic blood pressure; left descendens blood flow; total left descending coronary vascular resistance; left descending vessel element vascular resistance¹; left

1. Left descending vessel element vascular resistance is ((coronary perfusion pressure - peripheral coronary pressure) ÷ left descending Coronary arterial blood flow) expressed in units of Newton.sec.cm.⁻⁵ (as are all resistances). The bastard unit is used because of the inordinate size of the numbers when expressed in the customary units of Dyne.sec.cm.⁻⁵.

TABLE M-3

INFORMATION REGARDING MONGREL DOGS
USED IN THESE EXPERIMENTS

TABLE M-3A

CONTROL EXERCISES

DOG OR EXPERIMENT NO.	WEIGHT (KG.)	AGE (YEARS)	SEX	NUMBER OF INFUSIONS	OCCLUSION DURATION (MINUTES)
RC-1	9	1	♀	3	7
RC-2	8	2	♀	4	15
RC-3	9.5	0.3	♂	5	3.5
RC-4	11.5	1	♀	3	19
RC-5	15.5	2	♂	1	11
RC-6	10.5	0.5	♀	5	26
RC-7	10	10	♀	3	8

TOTAL

7 DOGS

24 INFUSIONS

TABLE M-3B

EXPERIMENTAL EXERCISES

DOG OR EXPERIMENT NO.	WEIGHT (KG.)	AGE (YEARS)	SEX	NUMBER OF INFUSIONS	OCCLUSION DURATION (MINUTES)
RE-1	6.5	14	♂	3	4
RE-2	5.5	2	♂	2	2.5
RE-3	6.5	1	♂	3	25
RE-4	6	1	♀	4	3
RE-5	6	2	♂	3	33
RE-6	7	2.5	♂	1	16.5
RE-7	9	2	♂	2	2
RE-8	8	2	♂	1	6
RE-8				2	16
RE-9	11	5	♂	1	1.5
RE-9				1	11.5

TABLE M-3B (cont.)

DOG OR EXPERIMENT NO.	WEIGHT (KG.)	AGE (YEARS)	SEX	NUMBER OF INFUSIONS	OCCLUSION DURATION (MINUTES)
RE-10	8	1	♂	1	36
RE-11	8.5	8	♀	2	14
RE-12	10	1	♀	1	15
RE-13	9.5	1	♀	1	28
RE-14	13.5	1	♂	3	5.5
RE-15	12.5	2	♀	1	14.5
RE-16	18	2	♀	4	8
RE-17	13.5	2	♂	1	5
RE-17				1	15
RE-17				1	25
RE-18	9.5	.3	♂	1	3.5
RE-19	12	2	♂	1	3.75
RE-19				1	13.75
RE-20	15.5	2	♂	1	13
RE-21	12.5	1	♂	1	11
RE-21				1	16

TOTAL

21 DOGS

45 INFUSIONS

CONTROL
EXPERIMENTAL

7 DOGS
21 DOGS

24 INFUSIONS
45 INFUSIONS

TOTAL

28 DOGS

69 INFUSIONS

descending peripheral coronary vascular resistance¹ in the territory of supply of the left descending coronary artery. These measurements were used to demarcate pre-infusion conditions.

B. Infusion Considerations

Having established a suitable pre-infusion base-line a five minute saline infusion was commenced. Similarly, a reasonable number of measurements was made during an infusion to obtain corresponding data for comparison with pre-infusion information.

C. Analysis of Infusion Information

Unpaired sample vectors for each parameter described above from each pre-infusion set and a corresponding infusion set were analysed statistically using the following significance of means "T" test for small sample numbers.

$$S = \sqrt{\frac{(\bar{X} - \bar{X})^2 + (\bar{X}' - \bar{X}')^2}{N + N' - 2}} \quad ((1))$$

$$T = \frac{\bar{X} - \bar{X}'}{S} \sqrt{\frac{N \times N'}{N + N'}} \quad ((2))$$

-
1. Peripheral coronary vascular resistance is (peripheral coronary pressure ÷ left descending Coronary arterial blood flow) expressed in units of Newton.sec.cm⁻⁵.

where $T = "t"$ value, $N + N' - 2 =$ degrees of freedom, $X =$ number of elements of the particular parameter vector of pre-infusion data, $X' =$ number of elements of corresponding infusion parameter vector, $\bar{X} =$ the difference between a particular element of X and the mean of X , $\bar{X}' =$ the difference between a particular element of X' and the mean of X' .

The routine was followed in cyclical fashion for each of the parameters: peripheral coronary pressure; aortic blood pressure; left descendens coronary blood flow; total left descendens vascular resistance; left descendens vessel element vascular resistance; and left descendens peripheral coronary vascular resistance. To facilitate execution of this routine, a computer program was written in APL/360 which was expanded to include in the output, statements relating to all parameters mentioned above: direction of change; significance of change; mean, variance, standard deviation, and standard error of the mean of all samples from before and during saline infusions. (See Appendix III for description of computer programme.)

These results were then sorted into two sets of data, each consisting of three parts; one, in which each of the three resistance parameters was seen to rise, and a second set in which each of the three resistance parameters was seen to fall. In each case these were tested according to the same routine to determine if any of the changes in any

of the resistance parameters in either direction were significant.

6. EXPERIMENTAL
(ADRENALINE (EPINEPHRINE))
INFUSIONS

General

Adrenaline¹ for experimental exercises was administered intravenously (at the rate of 0.19 μ /kg body wt/min. in concentration such that the delivery rate of saline solution from a Palmer infusion pump was 0.68 ml/min. from a 50 ml syringe) through the cannula in the left Femoral vein.

A. Pre-Infusion Considerations

Having established the manometric perfusion long-circuit, a reasonable number of measurements was made using the apparatus to determine: peripheral coronary pressure; aortic blood pressure; left descendens blood flow; total left descending coronary vascular resistance; left descending vessel element vascular resistance²; and left

1. Adrenaline; L Epinephrine-Bitartrate, Lot 125 B - 1340, Sigma Chemical Company, St. Louis, Missouri, U.S.A.

2. Vessel element vascular resistance is ((coronary perfusion pressure - peripheral coronary pressure) \div coronary blood flow) expressed in units of Newton.sec.cm⁻⁵. The bastard unit is used because of the inordinate size of the numbers when expressed in the customary units of Dyne.sec.cm⁻⁵.

descending peripheral coronary vascular resistance¹ in the territory of supply of the left descending coronary artery. These measurements were used to demarcate pre-infusion conditions.

B. Infusion Considerations

Having established a suitable pre-infusion base-line a five minute adrenaline infusion was commenced. Similarly, a reasonable number of measurements was made during an infusion to obtain corresponding data for comparison with pre-infusion information.

C. Analysis of Infusion Information

Unpaired sample vectors for each parameter described above from each pre-infusion set and a corresponding infusion set were analysed statistically according to the same routine for small sample numbers as was used in the control series. An identical analysis was performed on all the experimental (adrenaline) infusion data as was performed on the control (saline) infusion data.

7. TERMINATION OF EXPERIMENTS

On completion of each exercise, whether experimental

1. Peripheral coronary vascular resistance is (peripheral coronary pressure \div coronary blood flow) expressed in units of Newton.sec.cm⁻⁵.

or control, the experimental animal was slaughtered for humane reasons either by hemorrhage from the left femoral artery if the animal's blood pressure was sufficiently high on completion of the exercise, by the administration of an overdose of Nembutal, or by surgically removing the heart through a sternal split-incision. Following post mortem examination the carcasses were incinerated.

8. POST MORTEM EXAMINATIONS

At the termination of each experiment, the heart was removed surgically to ensure by inspection that the cannula in the coronary artery was properly intact. The cannula was flushed with ink-stained saline to ensure that it had been patent, to determine the extent of arterial collateral communications, and to assess the size of the territory of supply by the cannulated left descending coronary artery.

The aorta was examined to ensure that the cannula introduced through the right carotid artery was, in fact, in the Aortic arch.

RESULTS

GENERAL

The exercise of establishing the manometric perfusion long-circuit was attempted 38 times. Of these, 10 attempts resulted in failure. On one occasion a dog died on administration of the anesthetic. On another nine occasions fibrillation commenced on tampering with the heart. As the laboratory was not equipped with a cardiac defibrillator and direct cardiac massage proved fruitless, these nine animals became experimental mortality figures.

The mortality rate in these exercises was:

TABLE R-1

INFORMATION REGARDING MONGREL DOGS
USED IN THESE EXPERIMENTS

TABLE R-1A

CONTROL EXERCISES

DOG OR EXPERIMENT NO.	WEIGHT (KG.)	AGE (YEARS)	SEX	NUMBER OF INFUSIONS	OCCLUSION DURATION (MINUTES)
RC-1	9	1	♀	3	7
RC-2	8	2	♀	4	15
RC-3	9.5	0.3	♀	5	3.5
RC-4	11.5	1	♀	3	19
RC-5	15.5	2	♀	1	11
RC-6	10.5	0.5	♀	5	26
RC-7	10	10	♀	3	8

TOTAL

7 DOGS

24 INFUSIONS

TABLE R-1B

EXPERIMENTAL EXERCISES

DOG OR EXPERIMENT NO.	WEIGHT (KG.)	AGE (YEARS)	SEX	NUMBER OF INFUSIONS	OCCLUSION DURATION (MINUTES)
RE-1	6.5	14	♂	3	4
RE-2	5.5	2	♂	2	2.5
RE-3	6.5	1	♂	3	25
RE-4	6	1	♀	4	3
RE-5	6	2	♂	3	33
RE-6	7	2.5	♂	1	16.5
RE-7	9	2	♂	2	2
RE-8	8	2	♂	1	6
RE-8				2	16
RE-9	11	5	♂	1	1.5
RE-9				1	11.5

TABLE R-1B (cont.)

DOG OR EXPERIMENT NO.	WEIGHT (KG.)	AGE (YEARS)	SEX	NUMBER OF INFUSIONS	OCCLUSION DURATION (MINUTES)
RE-10	8	1	♂	1	36
RE-11	8.5	8	♀	2	14
RE-12	10	1	♀	1	15
RE-13	9.5	1	♀	1	28
RE-14	13.5	1	♂	3	5.5
RE-15	12.5	2	♀	1	14.5
RE-16	18	2	♀	4	8
RE-17	13.5	2	♂	1	5
RE-17				1	15
RE-17				1	25
RE-18	9.5	.3	♂	1	3.5
RE-19	12	2	♂	1	3.75
RE-19				1	13.75
RE-20	15.5	2	♂	1	13
RE-21	12.5	1	♂	1	11
RE-21				1	16

TOTAL

21 DOGS

45 INFUSIONS

CONTROL
EXPERIMENTAL

7 DOGS
21 DOGS

24 INFUSIONS
45 INFUSIONS

TOTAL

28 DOGS

69 INFUSIONS

$$\frac{1}{38} \times 100 = 2.63\% \text{ due to anesthetic reaction;}$$

$$\frac{9}{38} \times 100 = 23.68\% \text{ due to fibrillation following coronary occlusion; and}$$

$$\frac{10}{38} \times 100 = 26.31\% \text{ due to both causes.}$$

1. CONTROL EXERCISES

The control exercises were conducted as described in the Methods section with the following results.

The pre-infusion and infusion data collected using the methods described is presented in Tables RC-1 to RC-7 inclusive (see Appendix IV). The table numbers (Tables RC-1 to RC-7 inclusive) also refer to the dog or experiment numbers in Table R-1A from which the particulars of any control animal may be obtained. Table RC-8 presents the means of all values of control pre-infusion and infusion data sets depicted in Tables RC-1 to RC-7 inclusive, as well as the overall mean and the means of all cases in which each of the three resistance measurements were found to increase or decrease from pre-infusion levels. Table RC-9 depicts the direction of response and whether or not the response was a significant change from pre-infusion levels.

Examination of Table RC-9 indicates that on isolated occasions control infusions of saline solution were coincidental with significant change in one or more of the measured parameters (peripheral coronary pressure, aortic

TABLE RC-8

MEAN VALUES OF PERIPHERAL CORONARY PRESSURE, AORTIC BLOOD PRESSURE, LEFT DESCENDING BLOOD FLOW, CALCULATED RESISTANCE (TOTAL), CALCULATED VESSEL RESISTANCE, CALCULATED PERIPHERAL CORONARY RESISTANCE BEFORE AND DURING 5 MINUTE CONTROL INFUSIONS OF PHYSIOLOGICAL SALINE SOLUTION (0.67ml/min)

Pre-saline Infusion Means										Saline Infusion Means					
EXPT. NO.	OCCLUSION DURATION (min)	P.C.P. ² (mm Hg)	A.B.P. ³ (mm Hg)	FLOW ⁴ (ml/min)	C.R. ⁵ (Newton x sec. x cm ⁻⁵)	C.V.R. ⁶ x sec. x cm ⁻⁵	P.C.R. ⁷ cm ⁻⁵	R ² ⁸	P.C.P. (mm Hg)	A.B.P. (mm Hg)	FLOW (ml/min)	C.R. (Newton x sec. x cm ⁻⁵)	C.V.R. x sec. x cm ⁻⁵	I.C.R. (cm ⁻⁵)	R ²
RC-1-1 to RC-1-5	J.5	21.250	117.500	14.015	6.925	5.663	1.262	0.996	19.750	117.500	13.345	7.072	5.880	1.192	0.995
		21.000	114.000	12.225	7.451	6.078	1.372	0.909	21.500	116.000	10.775	8.786	7.151	1.636	0.994
		23.000	115.000	10.142	9.238	7.384	1.854	0.990	24.500	108.500	7.945	10.947	8.488	2.459	0.991
		20.000	101.250	8.630	9.859	7.912	1.947	0.994	20.500	103.500	6.637	12.504	10.021	2.483	0.992
		22.500	102.500	7.495	10.978	8.568	2.410	0.998	23.000	102.500	8.895	9.417	7.302	2.114	0.987
RC-1-1 to RC-1-5	7.0	19.000	64.167	5.212	10.384	7.310	2.994	0.973	19.000	52.500	4.660	9.484	6.076	1.404	0.970
		16.000	36.500	4.265	7.774	4.643	3.131	0.926	12.500	26.667	6.085	4.926	2.344	2.581	0.940
		6.500	20.167	3.232	5.265	3.578	1.687	0.979	4.200	20.833	2.918	6.910	5.975	0.936	0.984
		20.000	98.000	9.813	7.900	6.234	1.666	0.990	37.250	90.000	9.862	7.521	4.344	3.177	0.981
		15.250	94.000	6.397	11.950	9.973	1.977	0.990	14.000	77.600	5.934	13.335	10.922	2.412	0.984
RC-2-1 to RC-2-5	13.0	14.000	76.400	4.482	13.661	11.146	2.515	0.906	11.500	58.000	3.605	13.003	10.409	2.595	0.989
		15.000	96.500	2.274	33.968	28.685	5.282	0.982	13.750	90.250	7.301	10.326	8.754	1.572	0.975
		39.400	102.800	8.112	10.719	6.566	4.153	0.979	31.000	88.400	6.502	11.525	7.395	4.130	0.970
		27.500	77.000	4.850	13.779	8.687	5.092	0.971	25.000	61.600	3.296	17.084	10.010	7.074	0.950
		24.500	60.500	2.977	17.901	10.573	7.327	0.973	21.375	42.250	2.750	16.013	7.420	8.592	0.952
RC-3-1 to RC-3-5	19.0	22.833	40.333	1.573	20.952	8.900	12.051	0.970	21.667	34.667	1.200	23.053	8.645	14.404	0.994
		16.325	128.250	9.442	11.049	8.806	2.242	0.979	16.300	96.750	10.385	7.480	6.215	1.265	0.995
		16.125	99.250	11.422	6.949	5.817	1.131	0.966	16.100	99.500	12.142	6.542	5.483	1.059	0.996
		16.800	54.800	7.990	5.492	3.828	1.664	0.996	16.600	55.600	9.210	4.843	3.393	1.450	0.995
		21.000	84.000	9.664	4.600	3.207	1.394	0.995	20.800	80.800	10.486	4.244	2.961	1.283	0.994
RC-4-1 to RC-4-5	26.0	20.000	67.800	10.094	7.257	5.414	1.842	0.987	19.200	63.400	10.342	6.355	4.711	1.643	0.994
		18.800	63.000	8.892	5.451	3.839	1.613	0.998	19.200	63.400	9.006	5.627	3.922	1.705	0.996
		19.9847	81.9632	7.5527	10.6061	7.6951	2.9108	0.999	19.3424	75.8174	7.4544	9.8197	6.7720	1.695	0.997
		23.6058	93.1036	8.5274	10.0724	6.9362	3.1360	0.9843	21.9939	87.7262	7.3686	11.5262	7.9246	3.6017	0.9774
		18.4708	74.3764	7.5232	8.9949	6.5510	2.4439	0.9856	19.0687	68.1972	8.0616	7.9543	5.3823	2.5720	0.9411
RC-5-1 to RC-5-5		23.6760	97.9009	9.1596	9.0833	6.7576	2.3256	0.9870	22.0237	92.5498	7.9294	10.4783	7.8591	2.6193	0.9722
		18.8064	71.7577	7.0655	9.9127	6.7317	3.1829	0.9827	19.2686	65.6179	7.5338	9.1158	5.6333	3.4425	0.9841
		22.1156	88.4888	7.7391	10.9560	6.6186	3.3372	0.9852	22.6002	80.5094	6.7751	11.7466	7.7154	4.0307	0.9749
		19.2500	77.0917	8.4260	7.5423	5.5185	2.0238	0.9839	17.6350	74.3950	9.0311	6.9315	5.1662	1.7654	0.9842

1. Mean values are determined from the table in the Results section numbered correspondingly with the experiment numbers here.

2. P.C.P. is peripheral coronary pressure.

3. A.B.P. is aortic blood pressure.

4. FLOW is flow measured by manometric perfusion.

5. C.R. is total resistance (A.B.P. - P.C.P.) ÷ FLOW

6. C.V.R. is vessel element resistance ((A.B.P. - P.C.P.) ÷ FLOW)

7. P.C.R. is peripheral coronary resistance (P.C.P. ÷ FLOW)

8. R² is correlation coefficient squared. (See Appendix I for explanation of correlation coefficient).

TABLE RC-9

DIRECTION AND SIGNIFICANCE¹ (T-TEST) OF CHANGE IN MEAN VALUES OF PARAMETERS DISPLAYED IN TABLE RC-8 DURING 5 MINUTE CONTROL INFUSIONS OF PHYSIOLOGICAL SALINE SOLUTION (0.67 ml/min)

EXPT. NO.	OCCLUSION DURATION (min)	P.C.P. ² (mm Hg)	A.B.P. ³ (mm Hg)	FLOW ⁴ (ml/min)	C.R. ⁵ (Newton x sec. x cm ⁻⁵)	C.V.R. ⁶ (Newton x sec. x cm ⁻⁵)	P.C.R. ⁷ (Newton x sec. x cm ⁻⁵)
RC-3-1	3.5	(-)	(-)	(-)	(+)	(+)	(-)
RC-3-2		(+)	(+)	(-)	(+)	(+)	(+)
RC-3-3		(+)	(-)	(-)*	(+)	(+)	(+)*
RC-3-4		(+)	(+)	(-)	(+)	(+)	(+)
RC-3-5		(+)	(-)	(+)	(-)	(-)	(-)
RC-1-1	7.0	(-)	(-) Δ	(-)	(-)	(-)	(+)
RC-1-2		(-)	(-)*	(+)	(-)	(-)	(-)
RC-1-3		(-)	(+)	(-)	(+)	(+)	(-)
RC-7-1	8.0	(+) Δ	(-)	(+)	(-)	(-)*	(+)
RC-7-2		(-)	(-)	(-)	(+)	(+)	(+)
RC-7-3		(-)	(-) Δ	(-)*	(-)	(-)	(+)
RC-5-1	13.0	(-) Δ	(-) Δ	(+) Δ	(-) Δ	(-) Δ	(-) Δ
RC-2-1	15.0	(-) Δ	(-)*	(-)	(+)	(+)	(-)
RC-2-2		(-) Δ	(-)*	(-)	(+)	(+)	(+)
RC-2-3		(-) Δ	(-) Δ	(-)	(-)	(-)	(+)
RC-2-4		(-)*	(-)	(-)	(+)	(-)	(+)
RC-4-1	19.0	(-)	(-)	(-)*	(+)	(+)	(+)
RC-4-2		(-)	(-)	(+)	(-)	(-)	(-)
RC-4-3		(-)	(+)	(+)	(-)*	(-)*	(-)
RC-6-1	26.0	(-)*	(+)*	(+)*	(-)*	(-)*	(-)
RC-6-2		(-)	(+)	(+)	(-)	(-)	(-)
RC-6-3		(-)	(-)	(+)	(-)	(-)	(-)
RC-6-4		(-)	(-)*	(-)	(+)	(+)	(+)
RC-6-5		(-) Δ	(-)*	(-)	(-)	(-)	(+)
MEAN (ALL)		(-)	(-)	(-)	(-)	(-)	(+)
MEAN (CR+)		(-)	(-)	(-)	(+)	(+)	(+)
MEAN (CR-)		(+)	(-)	(+)	(-)	(-)	(+)
MEAN (CVR+)		(-)	(-)	(-)	(+)	(+)	(+)
MEAN (CVR-)		(+)	(-)	(+)	(-)	(-)	(+)
MEAN (PCR+)		(+)	(-)	(-)	(+)	(+)	(+)
MEAN (PCR-)		(-)	(-)	(+)	(-)	(-)	(-)

1. Changes are not significant ($P < 0.05$) unless specifically indicated.
 2. P.C.P. is peripheral coronary pressure.
 3. A.B.P. is aortic blood pressure.
 4. FLOW is flow measured by manometric perfusion.
 5. C.R. is total resistance ($A.B.P. \div FLOW$).
 6. C.V.R. is vessel element resistance ($(A.B.P. - P.C.P.) \div FLOW$).
 7. P.C.R. is peripheral coronary resistance ($P.C.P. \div FLOW$).
- * significant change at $P < 0.05$.
 Δ significant change at $P < 0.01$.

blood pressure, left descendens blood flow, total left descendens resistance, vessel element resistance and peripheral coronary resistance). However these cases of change were in both directions for all measured parameters and the mean overall effect was a decrease in all parameters except peripheral coronary resistance which increased. None of these mean changes achieved significant proportions even when divided into groups in which resistance directional changes were alike.

Examination of Table RC-9 indicates little correlation between periods of precedent occlusion of up to 26 minutes and direction of change or extent of change in any of the measured parameters coincident with intravenous infusion of physiological saline solution.

In these control exercises total resistance was seen to change significantly only on $3/24 \times 100 = 12.5\%$ of occasions and vessel element resistance and peripheral coronary resistance on $4/24 \times 100 = 16.7\%$ and $2/24 \times 100 = 8.3\%$ of occasions respectively.

2. EXPERIMENTAL EXERCISES

The experimental exercises were conducted as described in the Methods section with the following results.

The pre-infusion and infusion data collected using the methods described is presented in Tables RE-1 to RE-21 inclusive (see Appendix IV). The table number (Tables RE-1

TABLE RE-22

MEAN VALUES¹ OF PERIPHERAL CORONARY PRESSURE, AORTIC BLOOD PRESSURE, LEFT DESCENDING BLOOD FLOW, CALCULATED RESISTANCE (TOTAL), CALCULATED VESSEL RESISTANCE, CALCULATED PERIPHERAL CORONARY RESISTANCE BEFORE AND DURING 5 MINUTE EXPERIMENTAL INFUSIONS OF ADRENALINE (0.19 µg/kg/min) IN SALINE SOLUTION (DELIVERED AT 0.67 ml/min)

Pre-Adrenaline Infusion Means										Adrenaline Infusion Means									
EXPT. NO.	OCCLUSION DURATION (min)	P.C.P. ² (mm Hg)	A.B.P. ³ (mm Hg)	FLOW ⁴ (ml/min)	C.R. ⁵ (Newton x sec.)	C.V.R. ⁶ (Newton x sec. x cm ⁻⁵)	P.C.R. ⁷ (cm ⁻⁵)	R ² ⁸	P.C.P. (mm Hg)	A.B.P. (mm Hg)	FLOW (ml/min)	C.R. (Newton x sec.)	C.V.R. (Newton x sec. x cm ⁻⁵)	P.C.R. (cm ⁻⁵)	R ²				
RE-9-1	1.5	32.500	88.500	8.557	8.255	5.156	3.099	0.960	63.250	145.500	13.655	9.287	5.064	4.224	0.974				
RE-7-1	2.0	18.000	80.667	7.253	9.850	7.537	2.312	0.960	15.000	103.000	8.207	10.532	8.943	1.588	0.968				
RE-7-2	2.0	11.000	77.500	4.465	14.104	12.145	1.959	0.970	13.167	81.500	5.832	11.688	9.904	1.784	0.951				
RE-2-1	2.5	6.375	41.750	2.270	23.433	19.948	3.485	0.935	11.250	147.750	15.255	8.298	7.655	0.643	0.983				
RE-2-2	2.5	6.750	28.250	4.042	6.372	4.631	1.741	0.944	5.333	25.000	2.347	8.679	6.920	1.960	0.988				
RE-4-1	3.0	15.000	92.400	11.206	8.072	6.737	1.335	0.973	20.333	121.667	19.533	5.178	4.310	0.868	0.955				
RE-4-2	3.0	16.333	63.667	6.133	8.656	6.420	2.237	0.968	19.167	132.667	16.822	6.367	5.440	0.927	0.964				
RE-4-3	3.0	12.250	45.000	5.372	6.972	4.937	2.035	0.970	14.125	112.875	14.465	6.343	5.613	0.821	0.966				
RE-4-4	3.0	13.813	43.500	5.080	7.328	4.930	2.398	0.920	16.833	46.500	3.903	9.826	6.210	3.616	0.949				
RE-19-1	3.75	33.167	98.833	4.238	25.360	16.162	9.198	0.985	49.400	112.200	2.718	48.848	27.720	21.128	0.972				
RE-1-1	4.0	11.000	62.667	16.010	3.630	2.923	0.707	0.985	11.875	87.125	9.366	8.278	7.123	1.155	0.975				
RE-1-2	4.0	8.000	36.000	5.740	6.562	5.003	1.559	0.955	8.250	46.750	7.250	5.287	4.350	0.936	0.954				
RE-1-3	4.0	6.750	22.500	2.735	7.264	4.949	2.315	0.983	6.000	22.333	2.813	6.583	4.805	1.778	0.978				
RE-18-1	5.0	23.750	101.000	7.860	10.531	8.057	2.473	0.995	26.600	123.600	11.082	8.900	6.975	1.925	0.991				
RE-17-1	5.25	41.500	116.667	5.861	17.835	11.122	6.713	0.991	44.667	138.333	7.053	15.881	10.650	5.231	0.978				
RE-14-1	5.5	13.000	81.143	9.520	6.975	5.860	1.115	0.965	24.500	173.000	32.450	4.589	3.736	0.854	0.983				
RE-14-2	5.5	9.800	57.600	4.580	18.244	8.548	1.696	0.966	23.000	165.000	28.782	4.801	4.123	0.678	0.990				
RE-14-3	5.5	23.333	50.000	3.313	12.227	6.508	5.718	0.974	22.857	150.857	22.800	5.683	4.847	0.836	0.985				
RE-8-1	6.0	16.800	69.800	8.272	6.995	5.174	1.621	0.983	16.167	135.667	15.883	7.240	6.368	0.872	0.992				
RE-6-1	8.0	21.833	53.333	1.498	29.858	17.675	12.183	0.993	37.600	85.400	2.424	28.322	15.794	12.528	0.991				
RE-6-2	8.0	22.556	60.222	1.387	36.223	22.541	13.682	0.997	33.200	79.600	1.360	50.840	29.072	21.768	0.997				
RE-6-3	8.0	22.000	52.700	1.167	36.505	21.155	15.350	0.989	38.600	78.800	1.482	43.840	22.405	21.435	0.991				
RE-6-4	8.0	25.250	54.500	1.155	49.584	25.248	24.335	0.945	51.500	127.500	4.925	32.092	16.168	15.924	0.984				
RE-21-1	11.0	16.583	105.667	8.601	30.890	26.050	4.840	0.962	18.167	116.417	3.089	30.791	25.966	4.805	0.990				
RE-9-2	11.5	26.500	60.750	6.702	9.378	4.448	4.930	0.990	33.444	81.889	7.917	9.613	5.684	3.929	0.966				
RE-20-1	13.0	43.700	138.000	15.550	7.150	4.893	2.257	0.996	43.400	154.800	25.021	5.156	3.725	1.430	0.993				
RE-19-2	13.75	29.778	78.556	2.857	24.061	14.862	9.199	0.983	28.600	74.400	2.314	30.353	18.247	12.106	0.946				
RE-11-1	14.0	28.600	90.300	8.834	9.133	6.492	2.642	0.992	27.167	116.167	12.218	7.658	5.859	1.799	0.992				
RE-11-2	14.0	41.000	80.567	3.893	17.201	8.566	8.634	0.977	31.143	133.143	5.981	16.877	12.015	4.862	0.986				
RE-15-1	14.5	18.667	108.833	7.987	11.453	9.480	1.973	0.985	19.667	139.167	14.727	8.344	7.124	1.220	0.996				
RE-17-2	15.0	36.600	139.100	9.690	12.060	8.785	3.275	0.987	48.000	161.500	8.657	14.906	10.470	4.437	0.999				
RE-12-1	15.5	25.667	99.667	7.737	10.685	7.954	2.730	0.989	28.000	123.143	15.150	6.701	5.165	1.536	0.986				
RE-8-1	16.0	10.333	58.667	9.112	5.780	4.778	1.001	0.993	10.200	104.000	18.314	4.624	4.997	0.446	0.997				
RE-8-2	16.0	7.869	64.889	7.898	7.213	6.101	0.912	0.990	9.143	79.000	11.091	6.402	5.687	0.715	0.977				
RE-6-1	16.25	8.333	88.333	10.377	7.415	6.725	0.689	0.989	8.750	91.250	18.492	6.568	5.902	0.666	0.994				
RE-21-1	16.50	15.000	66.500	2.274	33.968	28.685	5.282	0.982	13.750	90.250	7.301	10.176	8.754	1.572	0.975				
RE-3-1	25.0	10.000	72.500	3.055	18.941	16.329	2.612	0.993	12.500	166.833	6.003	22.556	20.862	1.694	0.971				
RE-3-2	25.0	7.700	69.500	4.755	13.419	11.949	1.470	0.938	11.917	143.667	6.457	18.012	16.509	1.503	0.957				
RE-3-3	25.0	9.000	49.250	3.801	12.447	9.600	2.847	0.891	8.409	59.455	3.326	14.342	12.303	2.309	0.870				
RE-17-3	25.5	42.800	118.000	6.150	15.948	10.034	5.913	0.985	57.600	148.400	8.778	14.032	8.385	5.686	0.996				
RE-13-1	28.0	14.400	75.400	9.158	6.708	5.420	1.287	0.982	15.143	82.286	10.050	6.627	5.406	1.221	0.989				
RE-5-1	33.0	11.750	84.750	12.729	6.146	5.276	0.870	0.978	14.429	132.571	10.133	11.280	10.065	1.216	0.985				
RE-5-2	33.0	12.500	86.000	11.336	6.711	5.719	0.992	0.989	12.714	111.714	10.213	8.886	7.866	1.020	0.991				
RE-5-3	33.0	12.833	85.167	7.830	8.742	7.422	1.320	0.981	28.000	98.250	3.140	27.257	19.185	8.071	0.962				
RE-10-1	36.0	13.000	73.333	6.123	10.057	8.243	1.814	0.977	10.500	82.286	7.191	16.104	8.780	1.324	0.958				
MEAN (ALL)		18.896	75.556	6.526	14.185	10.035	4.150	0.977	23.627	109.182	10.355	14.202	10.052	4.151	0.976				
MEAN (CR+)		18.235	72.8444	6.5730	13.8148	9.6339	4.1806	0.9732	24.1143	101.3661	6.5417	19.2042	13.1472	6.0571	0.9692				
MEAN (CR-)		19.3359	79.1526	6.7228	14.3977	10.4081	3.9900	0.9816	23.2709	114.8944	13.1423	10.9422	7.7899	2.7574	0.9815				
MEAN (CVR+)		18.3498	71.0606	6.2797	13.9199	9.5695	4.3504	0.9739	22.0095	100.3237	6.5542	18.9452	13.1180	5.8272	0.9694				
MEAN (CVR-)		19.3359	79.1526	6.7228	14.3977	10.4077	3.9900	0.9739	24.9210	116.2694	13.3963	10.4061	7.5809	2.8093	0.9816				
MEAN (PCR+)		19.6271	73.6484	6.5126	16.0479	10.6563	5.3917	0.9763	28.5537	98.7305	5.5849	22.7725	14.4750	8.2976	0.9763				
MEAN (PCR-)		18.5682	76.4177	6.5319	13.3442	9.7547	3.5895	0.9770	21.4021	113.9027	12.5894	10.3320	8.0543	2.2777	0.9763				

1. Mean values are determined from the results table numbered correspondingly with the equivalent numbers here.

2. P.C.P. is peripheral coronary pressure.

3. A.B.P. is aortic blood pressure.

4. FLOW is flow measured by manometric perfusion.

5. C.R. is total resistance (A.B.P. ÷ FLOW).

6. C.V.R. is vessel element resistance ((A.B.P. - P.C.P.) ÷ FLOW).

7. P.C.R. is peripheral coronary resistance (P.C.P. ÷ FLOW).

DIRECTION AND SIGNIFICANCE (T-TEST)¹ OF CHANGE IN MEAN VALUES OF PARAMETERS DISPLAYED IN TABLE RE-22 DURING 5 MINUTE EXPERIMENTAL INFUSIONS OF ADRENALINE (0.19 μ /kg) IN PHYSIOLOGICAL SALINE SOLUTION (DELIVERED AT 0.67 ml/min)

EXPT. NO.	OCCLUSION DURATION (min)	P.C.P. ² (mm Hg)	A.B.P. ³ (mm Hg)	FLOW ⁴ (ml/min)	C.R. ⁵ (Newton	C.V.R. ⁶ x sec.	P.C.R. ⁷ x cm ⁻⁵)
RE-9-1	1.5	(+)Δ	(+)	(+)	(+)	(-)	(+)
RE-7-1	2.0	(-)	(+)Δ	(+)	(+)	(+)	(-)
RE-7-2	2.0	(+)	(+)	(+)	(-)	(-)	(-)
RE-2-1	2.5	(+)Δ	(+)Δ	(+)Δ	(-)	(-)	(-)*
RE-2-2	2.5	(-)*	(-)	(-)	(+)	(+)	(+)
RE-4-1	3.0	(+)Δ	(+)Δ	(+)*	(-)	(-)	(-)
RE-4-2	3.0	(+)Δ	(+)Δ	(+)Δ	(-)	(-)	(-)Δ
RE-4-3	3.0	(+)*	(+)Δ	(+)Δ	(-)	(+)	(-)Δ
RE-4-4	3.0	(+)Δ	(+)	(-)	(+)*	(+)	(+)*
RE-19-1	3.75	(+)Δ	(+)	(-)	(+)*	(+)*	(+)Δ
RE-1-1	4.0	(+)	(+)	(+)	(-)	(-)	(-)
RE-1-2	4.0	(+)	(+)*	(-)	(+)Δ	(+)Δ	(+)
RE-1-3	4.0	(-)	(-)	(+)	(-)	(-)	(-)
RE-18-1	5.0	(+)Δ	(+)Δ	(+)Δ	(-)*	(-)	(-)*
RE-17-1	5.25	(+)	(+)Δ	(+)	(-)	(-)	(-)
RE-14-1	5.5	(+)Δ	(+)Δ	(+)Δ	(-)Δ	(-)Δ	(-)
RE-14-2	5.5	(+)Δ	(+)Δ	(+)Δ	(-)Δ	(-)Δ	(-)Δ
RE-14-3	5.5	(-)	(+)Δ	(+)Δ	(-)Δ	(-)	(-)Δ
RE-8-1	6.0	(-)	(+)Δ	(+)*	(+)	(+)	(-)*
RE-16-1	8.0	(+)Δ	(+)Δ	(+)Δ	(-)	(-)	(+)
RE-16-2	8.0	(+)*	(+)*	(-)	(+)*	(+)	(+)*
RE-16-3	8.0	(+)Δ	(+)Δ	(+)*	(+)	(+)	(+)*
RE-16-4	8.0	(+)Δ	(+)Δ	(+)	(-)	(-)	(-)
RE-21-1	11.0	(+)Δ	(+)Δ	(-)	(-)	(-)	(-)
RE-9-2	11.5	(+)*	(+)Δ	(+)	(+)	(+)	(-)
RE-20-1	13.0	(-)	(+)*	(+)Δ	(-)Δ	(-)Δ	(-)Δ
RE-19-2	13.75	(-)	(-)	(-)	(+)	(+)	(+)
RE-11-1	14.0	(+)	(+)Δ	(+)*	(-)	(-)	(-)
RE-11-2	14.0	(-)	(+)Δ	(+)	(-)	(+)	(-)
RE-15-1	14.5	(+)	(+)Δ	(+)Δ	(-)	(-)	(-)*
RE-17-2	15.0	(+)Δ	(+)Δ	(-)	(+)*	(+)*	(+)*
RE-12-1	15.5	(+)Δ	(+)Δ	(+)Δ	(-)Δ	(-)Δ	(-)Δ
RE-8-1	16.0	(-)	(+)Δ	(+)Δ	(-)	(-)	(-)Δ
RE-8-2	16.0	(+)	(+)Δ	(+)	(-)	(-)	(-)
RE-6-1	16.25	(+)	(+)	(+)	(-)	(-)	(-)
RE-21-1	16.5	(-)Δ	(-)Δ	(+)Δ	(-)Δ	(-)Δ	(-)Δ
RE-3-1	25.0	(+)Δ	(+)Δ	(+)Δ	(+)	(+)	(-)Δ
RE-3-2	25.0	(+)Δ	(+)Δ	(+)*	(+)	(+)	(+)
RE-3-3	25.0	(-)	(+)*	(-)	(+)	(+)	(-)
RE-17-3	25.5	(+)*	(+)Δ	(+)*	(-)	(-)	(-)
RE-13-1	28.0	(+)	(+)*	(+)	(-)	(-)	(-)
RE-5-1	33.0	(+)Δ	(+)Δ	(-)	(+)*	(+)*	(+)
RE-5-2	33.0	(+)	(+)Δ	(-)	(+)*	(+)*	(+)
RE-5-3	33.0	(+)Δ	(+)Δ	(-)Δ	(+)Δ	(+)Δ	(+)Δ
RE-10-1	36.0	(-)*	(+)	(+)	(+)	(+)	(-)*
MEAN (ALL)		(+)	(+)Δ	(+)Δ	(+)	(+)	(+)
MEAN (CR+)		(+)	(+)Δ	(-)	(+)	(+)	(+)
MEAN (CR-)		(+)	(+)Δ	(+)Δ	(-)	(-)	(-)
MEAN (CVR+)		(+)	(+)Δ	(+)	(+)	(+)	(+)
MEAN (CVR-)		(+)	(+)Δ	(+)Δ	(-)	(-)	(-)
MEAN (PCR+)		(+)	(+)*	(-)	(+)	(+)	(+)
MEAN (PCR-)		(+)	(+)Δ	(+)Δ	(-)	(-)	(-)

1. Directional changes are not significant ($P < 0.05$) unless specifically indicated.
 2. P.C.P. is peripheral coronary pressure.
 3. A.B.P. is aortic blood pressure.
 4. FLOW is flow measured by manometric perfusion.
 5. C.R. is total resistance (A.B.P. \div FLOW).
 6. C.V.R. is vessel element resistance ((A.B.P. - P.C.P.) \div FLOW).
 7. P.C.R. is peripheral coronary resistance (P.C.P. \div FLOW).
- * significant change at $P < 0.05$.
Δ significant change at $P < 0.01$.

to RE-21 inclusive) also refers to the dog or experiment number in Table R-1B from which particulars of any experimental animal may be obtained. Table RE-22 presents the means of all values of experimental pre-infusion and infusion data sets depicted in Tables RE-1 to RE-21 inclusive, as well as the overall mean and the means of all cases in which each of the three resistance measurements were found to increase or decrease from pre-infusion levels. Table RE-23 depicts the direction of response and whether or not the response was a significant change from pre-infusion levels.

Examination of Table RE-23 indicates that on individual occasions adrenaline infusions were coincident with significant changes in one or more of the measured parameters (peripheral coronary pressure, aortic blood pressure, left descendens blood flow, total left descendens resistance, vessel element resistance and peripheral coronary resistance) and the mean overall effect was an increase in all measured parameters, significantly so in aortic blood pressure and left descendens blood flow. None of these mean changes achieved significant ($P < 0.05$) proportions even when divided into groups in which resistance directional changes were alike, excepting the cases of aortic blood pressure and left descendens blood flow.

Aortic blood pressure always rose significantly ($P < 0.05$) concomitantly with increased coronary blood flow. Left

CALCULATED TOTAL RESISTANCE (VESSEL ELEMENT RESISTANCE +
PERIPHERAL CORONARY RESISTANCE) EXPRESSED AS PERCENT OF
PRE-INFUSION LEVELS

EXPT. NO.	OCCLUSION DURATION (MINS)	C.R. ¹	C.V.R. ²	P.C.R. ³
RE-1-1	4.0	80.5600	115.0100	60.0700
RE-1-2	4.0	228.05	243.6600	163.5000
RE-1-3	4.0	90.6100	97.08	76.7900
RE-2-1	2.5	35.4116	38.3713	18.4578
RE-2-2	2.5	139.3443	149.4213	112.5617
RE-3-1	25.0	119.0824	127.7565	64.8481
RE-3-2	25.0	134.2293	138.1622	102.2431
RE-3-3	25.0	115.2212	128.1503	71.6319
RE-4-1	3.0	64.1435	63.9682	65.0285
RE-4-2	3.0	73.5492	84.7448	41.4307
RE-4-3	3.0	92.2903	113.7033	40.3501
RE-4-4	3.0	134.0884	125.9697	150.7609
RE-5-1	33.0	183.5372	190.7478	139.7701
RE-5-2	33.0	132.4003	137.527	102.8067
RE-5-3	33.0	311.7877	258.5008	611.2268
RE-6-1	16.25	88.5812	87.7621	96.5788
RE-7-1	2.0	106.9249	118.6613	68.6851
RE-7-2	2.0	82.8692	81.5524	91.0584
RE-8-1	6.0	103.4995	118.5009	53.7807
RE-8-2	16.0	80.0081	87.4561	44.4933
RE-8-3	16.0	88.7531	90.2616	78.3453
RE-9-1	1.5	112.4977	98.2013	136.291
RE-9-2	11.5	102.5098	127.8024	79.6832
RE-10-1	36.0	100.4692	106.5125	73.0064
RE-11-1	14.0	83.8488	90.2577	68.1012
RE-11-2	14.0	98.1158	140.2534	56.3123
RE-12-1	15.0	62.7127	64.9264	56.2639
RE-13-1	28.0	98.7997	99.7422	94.8645
RE-14-1	5.5	65.7962	63.7525	76.5779
RE-14-2	5.5	46.8665	48.2273	40.0153
RE-14-3	5.5	46.4804	74.4716	14.6271
RE-15-1	14.0	72.8564	75.1543	61.8179
RE-16-1	8.0	94.8543	89.3567	102.8299
RE-16-2	8.0	140.3515	128.9745	159.0957
RE-16-3	8.0	120.0938	105.9093	139.6439
RE-16-4	8.0	64.7223	64.0361	65.4359
RE-17-1	5.0	89.0456	95.7607	77.9171

-
1. C.R. is total left descending coronary resistance.
 2. C.V.R. is vessel element resistance (C.R. - P.C.R.).
 3. P.C.R. is peripheral coronary resistance.

TABLE RE-24 (cont.)

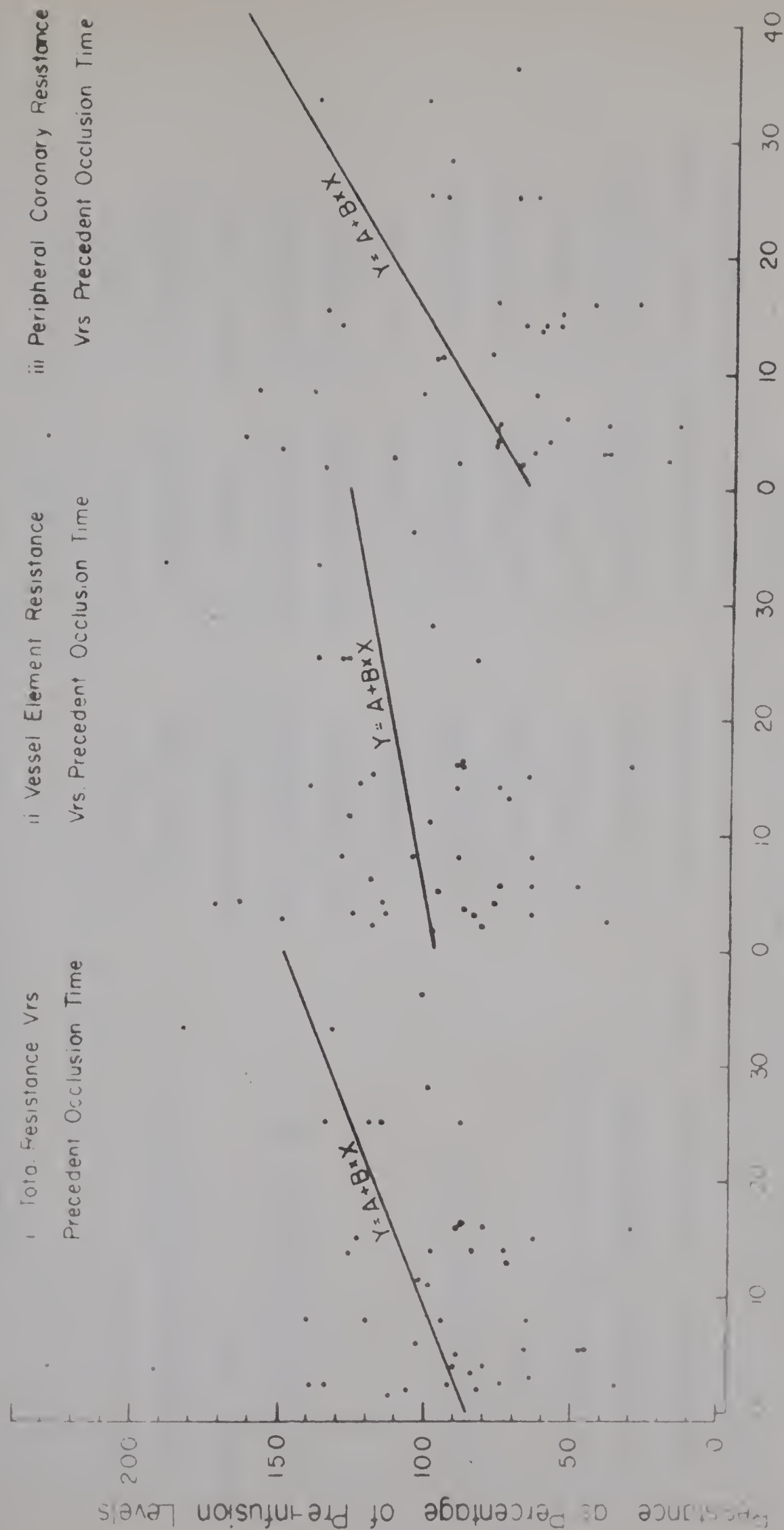
EXPT. NO.	OCCLUSION DURATION (MINS)	C.R.	C.V.R.	P.C.R.
RE-17-2	15.0	123.6008	119.1736	135.4857
RE-17-3	25.0	88.11	83.3632	96.1579
RE-18-1	3.5	84.5144	86.5603	77.849
RE-19-1	3.75	192.62	171.5125	229.7114
RE-19-2	13.75	126.1505	122.7776	131.6023
RE-20-1	13.0	72.1137	76.1378	63.3846
RE-21-1	11.0	99.6771	99.7543	99.2649
RE-21-2	16.0	30.398	30.5163	29.7593

descendens blood flow increased significantly ($P < 0.05$) with decrease in resistance and when resistance was seen to increase by non-significant proportions ($P > 0.05$) blood flow was seen to decrease by non-significant proportions ($P > 0.05$). The net effect being significant increases ($P < 0.05$) in aortic blood pressure and left descendens blood flow with only non-significant increases ($P > 0.05$) in all other measured parameters.

Table RE-24 lists the duration of occlusion prior to the experimental exercise of administering adrenaline infusions with the corresponding changes in the resistance parameters expressed as percentages of pre-infusion levels. Each measured parameter (total left descendens coronary resistance; coronary vessel element resistance, and peripheral coronary resistance) was tested for correlation with the duration of occlusion of the left descending Coronary artery prior to adrenaline infusion by the following method:

Occlusion times were considered as independent variables and each of the resistance parameters in turn were considered as dependent variables in scatter diagrams (see Fig. R-1). By the method of least squares the best straight line of the form $Y = A + B \times X$ was fitted where X was the independent variable and Y the dependent variable. The results (given in Table RE-25) indicate no significant correlation ($P > 0.05$) between duration

FIGURE R-1



Duration at Occlusion of Left Descendens Prior to Adrenaline Infusion (minutes)

TABLE RE-25

RESULTS OF TESTING FOR CORRELATION BETWEEN THE DURATION OF OCCLUSION
OF THE LEFT DESCENDENS AND THE RESISTANCE CHANGES CONCOMITANT WITH
ADRENALINE INFUSION ($0.19\mu\text{kg/min}$) (see Fig. R-1)

	C.R. ¹	C.V.R. ²	P.C.R. ³
mean of x = 1	12.21666667	12.21666667	12.21666667
standard deviation of x	9.946533201	9.946533201	9.946533201
mean of y =	104.4924709	107.3786526	98.22511549
standard deviation of y	49.81800927	45.07621951	88.95879864
A =	84.84935315	90.26024166	66.74080227
B =	1.607895045	1.401234185	2.5771607
standard error of B	0.723373069	0.6572357221	1.306050266
T value	2.222774294	2.132011602	1.973247712
standard error of estimate	47.72659003	43.36299147	86.17037182
correlation coefficient	0.3210281117	0.3091967892	0.2881537842
correlation coefficient squared	0.1030590485	0.09560265446	0.08303260336

1. C.R. is total left descending coronary resistance.
2. C.V.R. is vessel element resistance (C.R. - P.C.R.).
3. P.C.R. is peripheral coronary resistance.

of occlusion (1.5 - 36 minutes) of the left descending coronary artery and the concomitant changes in resistance of the vascular bed of the left descendens with infusion of adrenaline ($0.19 \mu/\text{kg}/\text{min.}$).

Examination of Table RE-23 indicates that in these experimental exercises total resistance was seen to change significantly on $15/45 \times 100 = 33.3\%$ of occasions and vessel element resistance and peripheral coronary resistance on $11/45 \times 100 = 24.4\%$ and $20/45 \times 100 = 44.4\%$ of occasions respectively.

3. COMPARISON OF CONTROL AND EXPERIMENTAL RESULTS

The incidence of significant changes in total resistance was almost 3 times as frequent ($33.3\%/12.5\% = 2.67$) during adrenaline infusions than during control saline infusions following precedent occlusion. Vessel element resistance and peripheral coronary resistance were almost 1.5 times as frequent ($24.4\%/16.7\% = 1.4$) and in excess of 5 times as frequent ($44.4\%/8.3\% = 5.3$) respectively during adrenaline infusions than during control saline infusions following precedent occlusion.

The occasion of change of total resistance during adrenaline infusions occurred in both directions with near equal frequency during control saline infusions. i.e. change

was only

$$\left(\frac{\frac{18 \text{ experimental increases in resistance}}{27 \text{ experimental decreases in resistance}}}{\frac{9 \text{ control increases in resistance}}{15 \text{ control decreases in resistance}}} = 1.1 \right)$$

1.1 times as frequent during adrenaline infusion than during control saline infusion. Resistance behaved not materially different under experimental conditions than in the control circumstances, with regard to direction of change.

CONCLUSIONS

A. Control Exercises

The control situation emerges quite clearly from examination of the results. Acute coronary (left descending Coronary artery) occlusion of a transient nature preceeding a non-chemically stimulating infusion (saline only) was concomitant with a variety of changes in calculated resistance of the left descending coronary vascular bed. These changes, which were equally bi-directional and in the mean not significant in magnitude, were following acute transient

occlusion (of the left descending Coronary artery) of varying duration (3.5 to 26.0 minutes). If these changes were any different from those which would occur at random in a normal anesthetized dog, then it could only be due to the effects of, establishing the manometric perfusion long circuit, and the imposition of transient coronary occlusions on the animals. Since there were no net changes in calculated resistance (of the left descending coronary vascular bed) it is reasonable to conclude that establishment of the preparation did not effect the manner in which the intrinsic resistance of this vascular bed fluctuates.

B. Experimental Exercises

From examination of the results certain conclusions can be arrived at, not the least of which is that establishment of the manometric perfusion long-circuit and the imposition of transient coronary occlusions of varying duration (1.5 to 36.0 minutes) does not effect the general systemic response of the anesthetized dog to intravenous infusions of adrenaline ($0.19 \mu/\text{kg}/\text{min.}$). Concomitant with adrenaline infusions aortic blood pressure and left descending coronary artery inflow always increased by significant proportions. This is the classic response (36).

Changes in resistance of the vascular bed of the left descendens were by no means so decisively classical. On 15 of 45 or $15/45 \times 100 = 33.3\%$ of the occasions where

total resistance of the left descendens vascular bed was seen to change significantly 8 or $8/15 \times 100 = 53.3\%$ of the changes were increases and 7 or $7/15 \times 100 = 46.7\%$ of the changes in resistance were decreases. These results are not conclusive but they would seem to be different from those obtained in control exercises where significant changes in resistance almost never occurred.

This much is clear, however. Two-thirds (66.7%) of the time, the resistance of the post-transient occlusion-ary coronary vascular bed is not materially changed by intravenous adrenaline infusions ($0.19 \mu/\text{kg}/\text{min.}$) and when it is altered, which is one-third of the time, (33.3% of the time) the change can be in either the direction of increase or decrease with near equal frequency.

It follows then (since control resistance did not change) that such significant changes as did occur (33.3% of all adrenaline infusions) were associated with the experimental factor, adrenaline.

Since, there was no significant correlation between duration of precedent occlusion (1.5 to 36.0 minutes) and changes in resistance (associated with adrenaline) of the left descendens vascular bed, and such changes as did occur were equally frequent in both directions, it can not be concluded that the transient coronary occlusions caused or precipitated only those changes associated with adrenaline

which were increases and not those which were decreases in resistance.

It can be concluded, however, that following acute transient occlusion of the left descending Coronary artery on 33.3% of occasions the intravenous infusion of adrenaline ($0.19 \mu/\text{kg}/\text{min.}$) does precipitate change in the resistance of the vascular bed of that artery.

Figure R-1¹ and Table RE-25² illustrate that there is very poor correlation between occlusion duration and the change of resistance in response to adrenaline infusion ($0.19 \mu/\text{kg}/\text{min.}$), but it does demonstrate a trend, however slight, which has the resistance of the left descendens vascular bed increasing with increased precedent left descending Coronary artery occlusion duration. This tendency for increase in resistance is only real in so far as resistance decreases tend, slightly, to be of less magnitude as precedent occlusion time increases. So, perhaps, there is some slight alpha (α) potentiation precipitated by the ischemic effect imposed by transient occlusion of the left descending coronary artery or some marginal effect of beta

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1. Results B. Experimental Exercises, Fig. R-1, Resistance as percent of pre-infusion levels vrs. precedent occlusion time.
 2. Results B. Experimental Exercises, Table RE-25, Results of testing for correlation between the duration of occlusion of the left descendens and the resistance changes concomitant with adreanline infusion ($0.19 \mu/\text{kg}/\text{min.}$).

blocade precipitated in the same way but the correlation was so poor that the position can not be maintained with sufficient confidence to conclude it from these data.

SUMMARY

1. Manometric perfusion is described. This is a new method which has been developed for the measurement of blood flow in a 'long circuit'. The left brachial artery is cannulated with a polyethylene tube which is then used to cannulate the anterior descending coronary artery. A side arm leads to a mercury manometric pressure perfusion head. The pressure was monitored by means of a standard transducer recording on a polygraph and used as described in the text.

This method enabled the following parameters of the long circuited coronary circulation to be measured:-

- A. the arterial pressure perfusing the anterior descending coronary artery;
- B. blood flow in the same vessel;
- C. the following two components of the total resistance of the vascular bed:-
 - (i). resistance of the vessels leading from the aorta to the anastomotic network of the myocardium;
 - (ii). resistance of the vessels - including the microcirculation - leading from the anastomotic network to the venous side of the coronary circulation;
- D. peripheral coronary pressure - i.e. the pressure recorded in a coronary artery distal to an occlusion. This is mainly pressure transmitted through collaterals from the intact coronary vessels.

2. Responses of the coronary vascular bed to adrenaline

In the nature of the method all observations are made after varying periods of coronary occlusion.

Two findings from previous work relate to the present findings -

- A. In the dog with an intact coronary circulation not exposed to the stress of occlusion, the normal reaction to intravenous adrenaline infusion is a decrease in vascular resistance to flow, partly due to adrenergic vasodilatation.
- B. In dogs in which a coronary artery has been occluded permanently, although there is flow in the regions distal to the occlusion, adrenaline reversal has been shown to occur. That is to say, intravenous infusion of adrenaline now produces vasoconstriction.

In the present work the heart had been subjected to the stress of operation. There were inevitably short periods of occlusion. The circulation was restored subsequently but through an extra-corporeal circulation. The following were the findings relating to the coronary responses to intravenous adrenaline:-

- (i). intravenously adrenaline was infused in doses of $0.19 \mu\text{g/Kg/min}$ for periods of 5 minutes. Forty-five infusions were carried out on 21 dogs.

- (ii). in 15.7% of all infusions vaso-dilatation occurred. In 17.6% of all infusions vaso-constriction occurred. In 66.7% of all infusions no significant change occurred.
- (iii). There were insufficient experiments for a final statement but the data suggested further that the extent of the adrenaline reversal is a function of the duration of the occlusion which preceded the infusion.

It was, therefore concluded that adrenaline reversal can be brought about by periods of anoxia such as follow temporary or permanent occlusion of a coronary artery. Short periods of occlusion may not, however, be consistent in their effect.

BIBLIOGRAPHY

1. Allen, J.B., J.R. Roodt The effect of the level of the ligature on mortality following ligation of the circumflex artery in the dog.
Am. Heart J. 39:273, 1950.
2. Anderson, F.F., A. Cameron A note on an air-activated pyren flowmeter for biological experiments.
J. Am. Pharm. Assoc. 39:183, 1950.
3. Anderson, F.F., B.N. Craver A pyren apparatus for the perfusion of the coronary circulation of mammalian hearts.
J. Pharmacol. & Exp. Therap. 93:135, 1935.
4. Andreyev, I.A. Arch. Neurol. and Psychiat. 34:481, 1935.
5. Anger, H.O., F.T. Upham In vivo counting methods in medical research.
Methods in Medical Research Chicago: Yr. Bk. Pub., Vol. 8, pp. 248-253, 1960.
6. Anrep, G.V. J. Physiol. 65:357, 1928.
7. Anrep, G.V., A. Blalock, M. Hammouda The distribution of the blood in the coronary blood vessels.
J. Physiol. 67, 87, 1929.
8. Anrep, G.V., M.R. Kenawy The coronary vasodilator action of khellin.
Am. Heart J. 37:531, 1949.
9. Anrep, G.V., H.N. Segall The regulation of the coronary circulation.
Heart, 13, 239, 1926.
10. Antopol, W., R. Rossler Ueber die Herzwirkung von Hypophysenhinterlappenextrakten am Hund unter natürlichen Kreislaufbedingungen.

- A. ges. exp. Med. 94, 453, 1934.
11. Baker, J.B.E. An improved apparatus for mammalian heart perfusion. J. Physiol. 115:30P, 1951.
12. Baldes, E.J., J.F. Herrick A thermostromuhr with direct current heater. Proc. Soc. Exp. Biol. Med. 37:432, 1937.
13. Barker, E.S., J.K. Clark Measurement of renal blood flow by application of the Fick principle. Methods in Medical Research Chicago: Yr. Bk. Pub. Vol. 8, pp. 283-292, 1960.
14. Baroldi, G., O. Mantero, G. Scmazzone The collaterals of the coronary arteries in normal and pathological hearts. Circ. Res. 4, 223, 1956.
16. Beck, C.S., V.L. Ticky The production of a collateral circulation to the heart. Am. Heart J. 10:849, 1935.
17. Berman, J.K., D.C. Fields, H. Judy, V. Mori, R. Palker Gradual vascular occlusion. Surg. 39:399, 1956.
18. Berne, R.M. Effect of epinephrine and nor-epinephrine on coronary circulation. Circ. Res. 6:644, 1958.
19. Berne, R.M., J.R. Blackmon, T.H. Gardner Arterial oxygen content and coronary blood flow. Federation Proceedings 14, 12, 1955.
20. Berne, R.M., J.R. Blackmon, T.H. Gardner Hypoxemia and coronary blood flow. J. Clin. Invest. 36, 1101, 1957.
21. Binet, L. M. Burnstein Sur une nouvelle methode

- de perfusion avec du sang
circulant.
C.R. Acad., Sci. Paris,
221, 197, 1945.
22. Bing, R.J. Determination of coronary
blood flow.
Methods in Medical Research
Chicago: Yr. Bk. Pub.
Vol. 8, pp. 269-275, 1960.
23. Bing, R.J., M.M. Hammond,
J.C. Handelsman, S.R.
Powers, J.F.C. Spencer,
J.E. Eckenhoff, W.T.
Goodale, J.H. Hafken-
schiel, S.S. Kety The measurement of coronary
blood flow, oxygen con-
sumption and efficiency
of the left ventricle in
man.
Am. Heart, 5, 38:1, 1949.
24. Blair, E. Anatomy of the ventricu-
lar coronary artery in the
dog.
Circ. Res. 9:333, 1961.
25. Blum, L. Gradual occlusion of the
coronary arteries.
Am. Heart J., 16:159-64,
1938.
26. Blumgart, H.L. Studies on the relation
of the clinical manifes-
tation of angina pectoris,
coronary thrombosis and
myocardial infarction to
the pathological findings.
Am. Heart J. 19:1, 1940.
27. Blumgart, H.L. Experimental production
of intercoronary arterial
anastomosis and their
functional significance.
Circulation 1:10-27, 1950.
28. Bradley, S.E. Estimation of hepatic
blood flow.
Methods in Medical Research
Chicago: Yr. Bk. Pub.,
Vol. 8, pp. 275-283, 1960.
29. Borcq, P. Note sur les arteres
coronaires.
Bull. Soc. Anat. 17:112-
117, 1920.

30. Bruner, H.D. (Editor) Peripheral blood flow measurement. I. Blood-tissue exchange methods. Methods in Medical Research Chicago: Yr. Bk. Pub., Vol. 8, pp. 222-292, 1960.
31. Burchell, H.B. Adjustments in coronary circulation after experimental coronary occlusion. Arch. Internal Med. 65: 240-262, 1940.
32. Busch, E. Eine Methode zur Erfassung von coronarvenenblut beim Kaninchen ohne Thoraxeröffnung und ihre Anwendung zur Untersuchung coronarerweiternder Stoffe. Arch. exp. Pathol. u. Phar. 237, 565, 1960.
33. Cameron, A., B.N. Craver A method with perfused feline hearts of quantitatively comparing drugs with coronary vasodilating activity. Proc. Soc. Exp. Biol. Med. 74:271, 1950.
34. Carslaw, H.S. The mathematical theory of the conduction of heat in solids. London, MacMillan, 1921.
35. Chardach, W.M. The mortality following ligation of the anterior descending branch of the left coronary artery in dogs. Am. Surg. 141:443, 1955.
36. Charlier, R. Measurement of Lumen Changes in the Coronary Vessels in Coronary Vasodilators. Volume 10 of the International Series of Monographs on Pure and Applied Biology. Pergamon Press, London, 1961.
37. Chase, R.E., C.F. DeGaris Arterial coronarie (Cordis)

- in the higher primates.
Am. J. Physiol. Anthropol.
24:427, 1939.
38. Christensen, G.C., F.L. Competi
Anatomic and functional studies of the coronary circulation in the dog and pig.
Am. J. Vet. Research
20:18, 1959.
39. Clark, L.C., Jr., R. Wolf, D. Granger, Z. Taylor
Continuous recording of blood oxygen tensions by polarography.
J. Applied Physiol.
6:189, 1953.
40. Conhein
Über die Folgen der Kranzarterienverschiessung für das Herz.
Arc. Path. Anat. Physiol.
85:503-37, 1881.
41. Conn, H.L., Jr.
Measurement of organ blood flow without blood sampling.
J. Clin. Invest. 34:916, 1955.
42. Conn, H.L., Jr.
Use of external counting techniques in studies of the circulation.
Symposium on Use of Indicators in the Study of the Circulation. Salt Lake City, Jan. 1961.
43. Conn, H.L., Jr., J.S. Robertson
Kinetics of potassium transfer in the left ventricle of the intact dog.
Am. J. Physiol. 181:319, 324, 1955.
44. Coulson, R.L., J. Grayson
Communication to the Royal Physiological Society.
July, 1968. Edinburgh Meeting.
45. Coulson, R.L., J. Grayson
Manometric Perfusion: A Communication to the XXIV International Congress of Physiological Sciences.

- Washington, D.C., 1968.
(In press).
46. Crittenden, E.C., R.E. Shipley
An electronic recording flowmeter.
Rev. Sci. Instr., 15, 343, 1944.
 47. Dawes, G.S., J.C. Mott, J.R. Vane
The density flowmeter, a direct method for the measurement of the rate of blood flow.
J. Physiol. 121, 72, 1953.
 48. Day, S.B., J.A. Johnson
The distribution of the coronary arteries of the rabbit.
Anat. Res. 132:633, 1958.
 49. Denison, A.B., M.P. Spencer, H.D. Green
A square wave electromagnetic flowmeter for application to intact blood vessels.
Circ. Res. 3:39, 1955.
 50. Denison, A.B., M.P. Spencer, H.D. Green
Effects of autonomic nerves and their mediators on the coronary circulation and myocardial contraction.
Circ. Research, 6, 633, 1958.
 51. Dietrich, S.
Blutversorgung und Aktionsstrom des Herzens.
Z. exp. Med. 90, 689, 1933.
 52. Diguglielmo, L.
Anatomic variations in the coronary arteries.
Acta. Paediat. 41:393, 1954.
 53. Dobson, E.L., G.F. Warner
Measurement of regional sodium turnover and their application to the estimation of regional blood flow.
Am. J. Physiol. 189:269-276, 1957.
 54. Dock, W.
The capacity of the coronary bed in cardiac hypertrophy.
J. Expt. Med. 74:177, 1941.

55. Donald, D.E., H.E. Essen
Studies on chronic effects of ligation of the canine right coronary artery. Am. J. Physiol. 176:431, 1954.
56. Dorner, J.
Fehlermöglichkeiten bei der Durchblutungsmessung mit der Diathermic-Thermometeruhr Nach H. Rein. Arc. Exp. Pathol. u. Phar. 220:490, 1953.
57. Dumke, P.R., C.F. Schmidt
Quantitative measurements of cerebral blood flow in the macaque monkey. Am. J. Physiol., 138, 421, 1943.
58. Eckenhoff, J.E., I.H. Hafenschiel, E.L. Foltz, R.I. Driver
Influence of hypotension on coronary blood flow, cardiac work and cardiac efficiency. Am. J. Physiol., 152, 455, 1948.
59. Eckenhoff, J.E., J.H. Hafkenschiel, M.H. Harmel, W.T. Goodale, M. Lubin, R.J. Binh, S.S. Kety
Measurement of coronary blood flow by the nitrous oxide method. Am. J. Physiol., 152:356, 1948.
60. Eckenhoff, J.E., J.H. Hafkenschiel, C.M. Landmesser
The coronary circulation in the dog. Am. J. Physiol. 148, 582, 1947.
61. Eckstein, R.W.
Coronary interarterial anastomosis on young pigs and mongrel dogs. Circ. Res. 2:460-470, 1954.
62. Eckstein, R.W.
Effects of exercise and coronary artery narrowing on coronary collateral circulation. Circ. Res. 5:230-35, 1957.
63. Eckstein, R.W., D.E. Gregg, W.H. Pritchard
The magnitude and time of development in the collateral circulation in

- occluded femoral, carotid, and coronary arteries.
Am. J. Physiol., 132, 351, 1941.
64. Eckstein, R.W., J.A. McEachen, J. Demming, W.B. Newberry
A special cannula for determination of blood flow in the left common coronary artery of the dog.
Science, 113:385, 1951.
65. Eckstein, R.W., G. Smith, M. Eleff, J. Demming
The effect of arterialization of the coronary sinus in dogs on mortality following acute coronary occlusion.
Circ. 6:16, 1952.
67. Elliot, E.C., E.L. Jones, C.M. Bloor, A.S. Leon, D.E. Gregg
Day to day changes in coronary haemodynamics secondary to constriction of the circumflex branch of the left coronary artery in conscious dogs.
Circ. Res. 22:237, 1968.
68. Evans, C.L., E.H. Starling
The part played by the lungs in the oxidation processes of the body.
J. Physiol. 46, 413, 1913.
69. Foltz, E.L., R.G. Page, W.F. Sheldon, A.S. Weiss, S.K. Wong, W.J. Tuddenham
Factors in variation and regulation of coronary blood flow in intact anesthetized dogs.
Am. J. Physiol. 162:521, 1950.
70. Fronek, A., V. Ganz
Measurement of flow in single blood vessels including cardiac output by local thermodilution.
Circ. Res. 8:175, 1960.
71. Gaddum, J.H., W.S. Paert, M. Vogt
The estimation of adrenaline and allied substances in blood.
J. Physiol. 108, 467, 1949.

79. Girling, F. Effects of intravenous and intra-arterial adrenaline and of adrenaline after Priscoline in hind limb of intact rabbit. Am. J. Physiol. 164:400, 1951.
80. Goodale, W.T., D.E. Hackel Measurement of coronary blood flow in dogs and man from rate of myocardial nitrous oxide desaturation. Circ. Res. 1:502, 1953.
81. Goodale, W.T., M. Lubin, W.G. Banfield Catheterization of the coronary sinus. Am. J. Med. Sci. 214:695, 1947.
82. Goodale, W.T., M. Lubin, J.E. Eckenhoff, J.H. Hafkenschiel Coronary sinus catheterization for studying coronary blood flow and myocardial metabolism.
83. Graham, G.R. The partitioning of coronary flow: the coronary sinus fraction. J. Physiol. 128, 19P. 1955.
84. Grant, R.T. The comparative anatomy of the cardiac coronary vessels. Heart, 13:285, 1926.
85. Grayson, J. Internal calorimetry in the determination of thermal conductivity and blood flow. J. Physiol. 118:54-72, 1952.
86. Grayson, J. Observations on thermal conductivity changes in infarcting muscle. Nature, 215, 767, 1967.
87. Grayson, J. The importance of the nerve supply to the coronary vessels in relation to myocardial ischemia and

- infarction.
Amer. Heart J. 73, 570-573, 1967.
88. Grayson, J., R.L.
Coulson, M. Irvine Observations on Arterial Collateral Communications in the Dog Heart. Microcirculation Conference. Göteborg, 1968.
89. Grayson, J., R.L.
Coulson, B.T. Winchester Manometric Perfusion: Blood flow measurement in extra-corporeal circuits. J. Appl. Physiol. 1968. (In press).
90. Grayson, J., M. Irvine Reactivity of cardiac receptors before and after acute coronary occlusion. Cardiovascular Research 1968. (In press).
91. Grayson, J., M. Irvine Further observations on infarction. Observations on the myocardial vasculature of the monkey following acute coronary occlusion. The role of the coronary collaterals in the dog during infarction. Cardiovascular Research 1968. (In press).
92. Grayson, J., M. Irvine,
J.R. Parratt, J.
Cunningham Vasospastic elements in myocardial infarction following coronary occlusion in the dog. Cardiovascular Research. 2, 54-62, 1968.
93. Grayson, J., T. Kinnear Observations on temperature, blood flow and heat production in the human liver to environment and to glucose and insulin administration. Clin. Sci. 22:125, 1940.
94. Grayson, J., B. Lapin Observations on the mechanisms of infarction in the dog after experimental

occlusion of the coronary artery.
Lancet, 1284-1288, 1966.

95. Grayson, J., D. Mendel Myocardial blood flow in the rabbit.
American Journal of Physiology, Vol. 200, 968-974, 1961.
96. Grayson, J., J. Parratt The effect of haemorrhage on myocardial blood flow in monkeys, dogs and rabbits.
Journal of Physiol. 169, 30-31, 1963.
97. Grayson, J., J. Parratt The effect of Bradykinin on blood flow and heat production in the myocardium.
Experimentia 19, 161, 1964.
98. Grayson, J., J. Parratt Observations of blood flow in the myocardium.
Acta Anatomica 416-424, 1965.
99. Grayson, J., J. Parratt A comparison of the effects of haemorrhage and amyl nitrite inhalation on myocardial metabolic heat production.
J. Physiol. 169, 30-31, 1965.
100. Grayson, J., J. Parratt Myocardial vascular reactivity after Beta-adrenergic blockade.
1966.

104. Gregg, D.E. The magnitude, adequacy and source of the collateral blood flow and pressure in chronically occluded coronary arteries.
Am. J. Physiol. 127:161-175, 1939.
105. Gregg, D.E. Coronary circulation in health and disease.
Lea and Febiger, Philadelphia, 1950.
106. Gregg, D.E. Blood supply to the heart.
Handbook of Physiology
Am. Physiology Soc.
Circ. Washington, D.C.
Section 2, pp. 1517-1584, 1963.
107. Gregg, D.E., E.M. Khouri, C.R. Rayford Systemic and coronary energetics in the resting unanesthetized dog.
Circ. Res. 16:102, 1965.
108. Gregg, D.E., F.H. Longino, P.A. Green, L.S. Czerwonka A comparison of coronary flow determined by the nitrous oxide method and by a direct method using the rotameter.
Circ. 3:89, 1951.
109. Gregg, D.E., W.H. Pritchard, R.W. Eckstein, A. Rotta, R.E. Shipley, J. Dingle, T.W. Steege, J.T. Wearn Observations on the accuracy of the thermistoruhr.
Am. J. Physiol. 136:250, 1942.
110. Gregg, D.E., W.E. Pritchard, R.E. Shipley, J.T. Wearn Augmentation of blood flow in the coronary arteries with elevation of right ventricular pressure.
Am. J. Physiol. 139:726, 1943.
111. Gregg, D.E., R.E. Shipley Augmentation of the left coronary inflow with elevation of left ventricular pressure observations

on the mechanism for increased coronary inflow with increased cardiac load.

Am. J. Physiol. 142, 44, 1944.

112. Gregg, D.E., R.E. Shipley

Studies on the venous drainage of the heart.

Am. J. Physiol. 151:13, 1947.

113. Gregg, D.E., R.E. Shipley, R.W. Eckstein, A. Rotta, J.T. Wearn

Measurement of mean blood flow in arteries and veins by means of the rotameter.

Proc. Soc. Exp. Biol. Med. 49, 267, 1942.

114. Gregg, D.E., J.J. Thorton, F.R. Mautz

The magnitude, adequacy and source of the collateral blood flow and pressure in chronically occluded coronary arteries.

Am. J. Physiol. 127:161, 1939.

116. Haight, C., M.M. Figley, H. Sloan, W.J. Ellsworth, J.A. Meyer, M.S. Berk, D.E. Boblitt

Coronary arteriography: I: Controlled experimental method; II: Modifications of coronary circulation. Circulation, 18, 732, 1958.

117. Halpern, M.H.

Arterial supply to the nodal tissue in the dog heart.

Circ. 9:547, 1954.

118. Halpern, M.H.

Blood supply to the atrioventricular system of the dog.

Anat. Rec. 121, 753, 1955.

119. Halpern, M.H.

The dual blood supply of the rat heart.

Am. J. Anat. 101:1, 1957.

120. Hanna, C.

The use of polybinylnp-rolidone in the assay of

- coronary active drugs.
Arch. Int. Pharmacodyn.
119:305, 1959.
121. Hanna, C., J.H. Shutt
Papaverine analogs. VI
Relationship between
chemical structure and
coronary vasodilator ac-
tion.
Arch. Exp. Pathol. u.
Pharmacol.
220:43, 1953.
122. Hansen, A.T., B.F.
Haxholdt, E. Husfeldt,
N.A. Lassen, O. Munck,
H.R. Sorenson, K.
Winkler
Measurement of coronary
blood flow and cardiac
efficiency in hypo-
thermia.
Scand. J. Clin. & Lab.
Invest. 8, 182, 1956.
123. Harris, A.S.
Delayed development of
ventric ectopic rhythms
following experimental
coronary occlusion.
Circ. 1:1318, 1950.
124. Hensel, H.J., K.
Golenhofen
Fortlaufende Registrier-
ung der Muskeldurchblutung
am Menschen mit einer
calorimetersonde.
Pfuger's Archiz. ges
Physiol. 259:267, 1954.
125. Hershgold, E.J., S.H.
Steiner, L.A. Saperstein
Distribution of myocardial
blood flow in the rat.
Circ. Res. 7:551, 1959..
126. Heuber, W., R. Mancke
Methods fur vergleichende
pharmakologische Unter-
suchungen an warmbluter-
herzen in der Anordnung
nach Landendorff. Aber-
halden's Handbuch der
biologischen Arbeitsmetho-
den, Urban und. Schwark-
zenberg, Berlin und Wien,
Abt. V., Teil, 8, 885,
1935.
127. Hitsh
Koronarkreislauf und Herz-
muskelarternien-Duet. Med.
Wochschr. 33:790-95, 1907.

128. Hudson, C.L. J. Exper. Med. 56:919, 1932.
129. Hyman, C. Peripheral blood flow measurements: Tissue clearance. Methods in Medical Research Chicago: Yr. Bk. Pub. Vol. 8, 256-242, 1960.
130. Jaimet, C.H., R.H. Tomlinson, L. Donato, G. Debus, P.F. Nace Inhalation radiocardiography. Second United Nations International Conference on the Peaceful Uses of Atomic Energy Paper No. A/CONF. 15/P/215.
131. James, T. Anatomy of the coronary arteries. New York: Hober, 1961.
132. James, T.N. The atrial coronary arteries in man. Circ. 17:90, 1958.
133. James, T.N. Blood supply of the human interventricular septum. Circulation 17:391, 1958.
134. Jardetzky, O. Oxygen consumption of the completely isolated dog heart in fibrillation. Circ. Research 4:144, 1956.
135. Jaques, R., J. Tripod, R. Meier Wechselwirkungen zwischen Schwermetallsalzen insbesondere Kupfersalzen und verschiedenen Pharmaka an den Coronargefassen des isolierten Herzens. Arch. exp. Pathol. u. Pharmacol. 230:26, 1957.
136. Johnson, J.R., C.J. Wiggers The alleged validity of coronary sinus outflow as a criterion of coronary reactions. Am. J. Physiol. 118, 38, 1937.
137. Jourdan, F., G. Faucon Etude experimentale de

l'action de la khelline
et de quelques uns de
ses derives sur le debit
coronaire.

Arch. Mal. Coeur et
Vaiss.

50, 748, 1957.

138. Jourdan, F., G. Faucon

Action sur le debit coro-
naire de chlorhydrate de
diethylamino-ethoxy-8-
hydroxyl-5-methyl-2-
furochromone.

Therapie, 12, 927, 1957.

139. Jourdan, F., G. Faucon

Valeur respective de
quelques derives xanthi-
ques comme coronaro-
dilatateurs.

Arch. Int. Pharmacodyn.
116, 423, 1958.

140. Jourdan, F., G. Faucon

Action sur le debit cor-
onaire de la methyl-3-
chromone.

Therapie 13, 635, 1958.

141. Kattus, A.A., D.E. Gregg

Some determinants of
coronary collateral blood
flow in the open chest
dog.

Circ. Res. 7:628, 1959.

142. Katz, G.

Neue Moglichkeiten zur
Aufzeichnung der Gefass-
weite von isoliert
durchstromten Organen.

Arch. Int. Pharmacodyn.
49:239, 1935.

143. Katz, L.N., K. Jochim,
A. Bohning

The effect of the extra-
vascular support of the
ventricles on the flow
in the coronary vessels.
Am. J. Physiol. 122, 236,
1938.

144. Katz, L.N., K. Jochim,
W. Weinstein

The distribution of the
coronary blood flow.
Am. J. Physiol. 122, 252,
1938.

145. Katz, L.N., E. Lindner The action of excess Na, Ca, and K on the coronary vessels.
Am. J. Physiol. 124:155, 1938.
146. Katz, L.N., E. Lindner The reaction of the coronary vessels to drugs and other substances.
J. Am. Med. Assoc. 113, 2116, 1939.
147. Katz, L.N., E. Lindner, W. Weinstein, D.J. Abramson, K. Jochim Effects of various drugs on the coronary circulation of the denervated isolated heart of the dog and cat.
Arch. Int. Pharmacodyn. 59:399, 1938.
148. Katz, L.N., W. Weinstein, K. Jochim The variability in the distribution of the outflow from each of the three major coronary arteries.
Am. J. Physiol. 113, 76, 1935.
149. Kety, S.S. Theory of blood-tissue exchange and its application to measurement of blood flow.
Methods in Medical Research Chicago: Yr. Bk. Pub., Vol. 8, pp. 223-227, 1960.
150. Kety, S.S. Measurement of local blood flow by the exchange of diffusible substance.
Methods in Medical Research Chicago: Yr. Bk. Pub., Vol. 8, pp. 228-236, 1960.
151. Kety, S.S., M.H. Harmel, H.T. Broomel, C.B. Rhose The solubility of nitrous oxide in blood and brain.
J. Biol. Chem. 173:487, 1948.
152. Kety, S.S., C.F. Schmidt The determination of cerebral blood flow in man by the use of nitrous oxide in low concentration

Am. J. Physiol. 143:53,
1945.

153. Khouri, E.M., D.E.
Gregg, C.R. Rayford

Effect of exercise on
cardiac output, left
coronary flow and myo-
cardial metabolism in
the unanesthetized dog.
Circ. Res. 16-17, 427,
1965.

154. Kiese, M., G. Lange

Calorimetrische Messung
der Durchblutung der
Herzmuskels.
Arch. Exp. Pathol. u.
Pharmakol., 231:149,
1957.

155. Kiese, M., G. Lange,
K. Resag

Die Wirkung von 2,6-Bis
(dianthanol-amino)-4,8-
dipiperidino-pyrimido
(5,4-d) pyrimidin auf
die Durchblutung des
experimentellen Herzin-
farkts und des gesunden
Herzmuskels.
Z. ges. exp. Med. 132:426,
1960.

156. Kountz, W.B.

Studies on the coronary
arteries of the human
heart.
J. Pharmacol. and exp.
Therap. 45:65, 1932.

157. Lafontant, R., H.
Feinberg, L.N. Katz

Coronary sinus method as
an adequate measure of
left ventricular coronary
flow and metabolism.
Circ. 22:774, 1960.

158. Lambertsen, C.J., S.N.
Owen

Continuous constant rate
sampling modification of
nitrous oxide method for
cerebral blood flow
in man.
Methods in Medical Research
Chicago: Yr. Bk. Pub.
Vol. 8, pp. 262-269, 1960.

159. Lange, G.

Messung der Durchblu-
tung im Herzinfarkt.

Arch. Exp. Pathol. u.
Pharmakol. 236:225, 1959.

160. Langendorff, O. Untersuchungen am uber-
lebenden Saugethierherzen
Pflugers Arch. ges.
Physiol. 61:291, 1895.
161. Larsen, V. An apparatus for measuring
the effect of drugs on the
coronary vessels in the
isolated heart.
Acta. Pharmacol. and
Tonicol. 4:1, 1948.
162. Laurie, W. Interarterial coronary
anastomosis in three
race groups.
Lancet I, 13-17, 1962.
163. Laurie, W., J.D. Woods Anastomosis of the coronary
circulation.
Lancet 2, 812-816, 1958.
164. Lecomte, J., H. Mazzella,
E. Vanremoortere Action des antihistamini-
ques de synthese et des
anesthésiques locaux
sur le débit coronarien
du cœur isolé de lapin.
Arch. exp. Physiol. 60:8,
1952.
165. Leitch, J.R., T.J.
Haley A note on the use of the
Anderson-Craver heart
perfusion apparatus.
J. Am. Pharm. Assoc.
41:512, 1952.
166. Lendrum, B., B. Kondo,
L.N. Katy The role of Thesbian
drainage in the dynamics
of coronary flow.
Am. J. Physiol. 143:243,
1945.
167. Lindner, A., M. Loudon,
G. Weiner Zur pharmakologischen
Beurteilung von coronar-
gefässerweiternden Stoffen.
Schweiz. med. Wschr. 83:
360, 1953.
168. Linzell, J.L. Internal calorimetry in
the measurement of blood

flow with heated thermocouples.

J. Physiol. 121, 390-402, 1953.

169. Lu, F.C., M.G. Allmark,
E.J. Carmichael, D.B.
MacMillan, A. Lavallee

The assay of some coronary dilator drugs in isolated mammalian hearts and dog hearts in situ.

J. Pharm. and Pharmacol. 5, 94, 1953.

170. Lu, F.C., K.I. Melville

A new apparatus procedure for continuous registration of changes in coronary flow concurrently with changes in heart contractions. J. Pharmacol. and Exp. Ther., 99, 277, 1950.

171. Ludena, F.P., E.
Miller, W.A. Wilt

A new perfusion apparatus for the study of the effects of drugs on the coronary vessels.

J. Am. Pharm. Assoc. 44:363, 1955.

172. Lumb, G.

The cardiac conduction tissue and its blood supply in the dog.

Am. J. Pathol. 35:467, 1959.

173. Mack, R., D. Nolting,
M. Kirsch, E. Luthy,
J.D. Choudhury, R.J.
Bing

Coronary blood flow determinations with radioactive rubidium. Second U.N. International Conference on the Peaceful Uses of Atomic Energy, Geneva, Paper No. A/CONF. 15/P/880, 1958.

174. Mantero, O., G. Baroldi,
G. Scmazzone

The coronary arterial circulation in the hypertrophic heart. Cardiologia 32:48-60, 1958.

175. Markwalder, J., E.H.
Starling

A note on some factors which determine the blood flow through the coronary circulation.

J. Physiol. 47, 275, 1913.

176. Mautz, F.R., D.E. Gregg Dynamics of collateral circulation following chronic occlusion of coronary arteries. Proc. Soc. Exptl. Biol. Med. 36:797-801, 1937.
177. May, A.M. Surgical anatomy of the coronary artery. Disease of Chest 38:645, 1960.
178. Melville, K.I., I. Mazurkiewicz Actions of potassium and calcium on coronary flow and heart contractions with special reference to the responses to epinephrine and norepinephrine. J. Pharmacol. and exp. Therap. 118, 249, 1956.
179. Meyer, F. Hat g-Strophantin eine Einwirkung auf den Coronarkreislauf. Med. Klin. 21, 869, 1912.
180. Meyer, O.B. Ueber einige Eigenschaften der Gefassmuskulatur mit besonderer Berucksichtigung der Adrenalin Wirkung. Z. Biol. 48:352, 1906.
181. Moe, G.K., M.B. Visscher The distribution of coronary blood flow. Blood, Heart, and Circulation. A.A.A. Sci. Public, 13, 100, 1940.
182. Morawitz, P., A. Zahn Ueber den Koronarkreislauf am Herzen in situ. Zentralbl. Physiol. 26, 465, 1912.
183. Muller-Mohnssen, H. Sie Topographie der Septumarterien im menschlichen Herzen und ihre Bedeutung fur die Entstehung von Killateralkreislauf bei Coronarsklerose. Beitr. Pathol. Anat. All. Pathol. 118:121, 142, 1957.

184. Olleon, J. Valeur comparee de quelques medications coronarodilatatrices (etude experimentale). (Ed. by A. Rey) p.133, 1957. Thèse de Lyon.
185. Olmstead, F., I.H. Page Haemodynamic changes in dogs caused by pentobarbital anesthesia. Am. J. Physiol. 210:817, 1966.
186. Parratt, J.R. Blockade of sympathetic receptors in the myocardial circulation. Brit. J. Pharmacol. 24: 601, 611, 1965.
187. Parratt, J.R., J. Grayson Myocardial vascular reactivity after beta-adrenergic blockade. Lancet I, 338-340, 1966.
188. Pianetto, M.B. The coronary arteries of the dog. Am. Heart J. 18:403-410, 1939.
189. Pitt, B. Interarterial coronary anastomosis. Circulation 20:816-822, 1959.
190. Polaceky, P. Svalove mitsky a poutka na vencithck tepnock u clovela Ceskoslov Morfol. 7:119, 1959.
192. Porter, W.T. Results of ligation of the coronary artery. J. Exptl. Med. 1:46-70, 1896.
193. Porter, W.T. A new method for the study of the isolated mammalian heart. Am. J. Physiol. 1:511, 1898.

194. Prinzmetal, M. The collateral circulation of the normal human heart by coronary perfusion with radioactive erythrocytes and glass spheres.
Am. Heart J. 33:420-442, 1947.
195. Provenza, V., S. Scherlis Coronary circulation in dog's heart.
Circulation Research, Vol. VII, No. 3, May, 1959.
196. Provenza, V., S. Scherlis Demonstrations of muscle sphincters as a capillary component in human heart.
Circ. 20:35, 1959.
197. Race, G.J., W.L.J. A large whale heart.
Edwards, E.R. Halden, Circ. 19:928, 1959.
H.E. Wilson, F.J.
Luibel
198. Ravin, A., E.F. Guver Coronary arteriosclerosis. Coronary anastomosis and myocardial infarction.
Arch. Internal Med. 78:125, 1946.
199. Rein, H. Die Thermo-Stromuhr. Ein Verfahren zur fortlaufenden Messung der mittleren absoluten Durchflussmengen in unteroffneten Gefassen.
in situ.
Z. Biol. 87:394, 1927-28.
200. Richardson, A.W., E.F. A newly modified electromagnetic blood flowmeter capable of high fidelity flow registration.
Denison, H.D. Green Circ. 5, 430, 1952.
202. Robertson, J.S. Mathematical treatment of uptake and release of indicator substances in relation to flow analysis in tissues and organs.

Handbook of Physiology
Section II, Circulation
Vol. I, American Physiol.
Society, Washington, D.C.
1962.

203. Rodbard, S., G.R.
Graham, F. Williams
Continuous and simultaneous
measurement of total
coronary flow, venous
return and cardiac output
in the dog.
J. Appl. Physiol. 6, 311,
1953.
204. Ryser, H., W. Wilbrandt
Die Wirkung von Recosen
auf den coronarwider-
stand der nach Langendorff
perfundierten Meerschwe-
inchenherzens und ihre
Deutung im Sinne eines
Verdrängungsantagonismus.
Arch. Int. Pharmacodyn.
96:131, 1960.
206. Sapirstein, L.A.
Measurement of the myo-
cardial blood flow in the
closed chested rat and the
effect of drugs and hemor-
rhage.
Circulation 18, 775, 1958.
207. Sapirstein, L.A., E.
Ogden
Theoretic limitations of
the nitrous oxide method
for the determination of
regional blood flow.
Circ. Res. 4:245, 1956.
208. Sayen, J.J., A.H.
Katcher, W.F. Sheldon,
C.M. Gilbert
The effect of heparterenal
on polarographic myocardial
oxygen, the epicardial
electrocardiogram and
contraction.
Circ. Res. 8:109, 1960.
209. Schlesinger, M.J.
An injection plus dissec-
tion study of coronary
artery occlusions and
anastomosis.
Am. Heart J. 15:528, 1938.

210. Schofield, B.M., J.M. Walker
Perfusion of the coronary arteries of the dog.
J. Physiol. 122, 489, 1953.
211. Sevelius, G., P.C. Johnson
Myocardial blood flow determined by surface counting and ratio formula.
J. Laf. Clin. Med. 54, 669, 1959.
213. Shipley, R.E., E.C. Crittenden
An optical recording rotameter for measuring blood flow.
Proc. Soc. Exp. Biol. Med. 56, 103, 1944.
215. Shipley, R.E., K.G. Kohlstaedt, R. Wegria
Pharmacology of the coronary circulation.
Pharmacological Reviews 3, 197, 1951.
216. Shipley, R.E., C. Wilson
An improved recording rotameter.
Proc. Soc. Ex. Biol. Med. 78, 724, 1951.
217. Singer, R.
The coronary arteries of the Bantu heart.
S. African Heart Med. J. 33:310, 1959.
218. Sobin, S.S.
Vasa vasorum of the pulmonary artery of the rabbit.
Circ. Research 11:257, 1962.
219. Sokoloff, L.
Quantitative measurements of cerebral blood flow in man.
Methods in Medical Research Yr. Bk. Pub., Vol. 8, pp. 253-261, 1960.
220. Sones, T.
Conecardioangiography clinical cardio-pulmonary physiology. New York:

Grune and Stratton, pp.
130-144, 1960.

221. Soskin, S., W.S. Priest,
W.J. Schultz The influence of epine-
phrine upon the exchange
of sugar between blood
and muscle.
Am. J. Physiol. 108, 107,
1934.
222. Stehle, R.L. A method for studying
variations in coronary
inflow during a series
of cardiac cycles, or
for determining inflow
rates generally.
J. Pharmacol. and exp.
Therap. 46:471, 1932.
223. Steiner, S.H., J.R.
Calvin The effects of anesthesia
with pentobarbital on Hemo-
dynamics and arterial
blood gases in splenec-
tomized dogs.
Journal of Thoracic and
Cardiovascular Surgery.
54:592, 1967.
224. Stenikar, I., T.
Zanolini Proprieta farmacologicke
di alcuni nuovi coronaro-
dilatatori ed in parti-
colare del flavon-7-os-
siacetato de etile.
II Farmaco - Ed. Sci.,
11, 855, 1956.
226. Tepperman, J. Effects of exercise and
anemia on coronary arteries
of small animals as re-
vealed by the corrosion-
cast technique.
Circ. Res. 9:576-84, 1961.
227. Thornton, J.J., D.E.
Gregg Effect of chronic cardiac
venous occlusion on
coronary arterial and
cardiac venous hemo-
dynamics.
Am. J. Physiol. 128:179,
1939.

228. Tripod, J., R. Meier
Wirkung von Serpasil (Reserpin, ein neues Alkaloid von Rauwolfia serpentina b.) auf isolierte Kreislauforgane.
Arch. Int. Pharmacodyn. 97:251, 1954.
229. Tripod, J., R. Meier
Determination et classification pharmacodynamique de l'action vasculaire peripherique de l'Apresoline du Nepresol et du Serpasil.
Arch. Int. Pharmacodyn 99:104, 1954.
230. Truitt, E.B.
A note on a modification of the Anderson-Craver perfusion apparatus for interchanging perfusion fluids.
J. Am. Pharm. Assoc. 44: 382, 1955.
231. Uhlmann, F., F. Nobile
Verbesserte Versuchsanordnung für Arbeiten mit dem isolierten Säugetierherzen.
Arch. Exp. Pathol. u. Pharmacol. 192:189, 1938.
233. Vane, J.R.
A new perfusion method.
J. Physiol. 121, 97, 1953.
234. Vasko, J.S., J. Gutelius, D.C. Sabiston
A study of predominance of human coronary arteries determined by arteriographic and perfusion techniques.
Am. J. Cardiol. 8:379, 1961.
235. Vanremortere, E., J. Lecomte, H. Mazzella, F. Nelomans
Action de l'histamine sur le débit coronaire du cœur isolé de lapin en fibrillation ventriculaire.

Acta Cardiologica 95:
466, 1953.

236. Vastesaeger, M., P.
Van Der Straeten, J.
Friart, G. Cardaele,
A. Ghys, R.M. Bernard
Les anastomoses inter-
coronaires telles qu'elles
apparaissent a la coronog-
raphie post mortem.
Acta Cardiologica
12:365-401, 1957.
237. Vera, L.B., de, E.
Corday, H. Gold
Drop meter: a simple de-
vice for measuring coro-
nary artery flow.
Circulation 16, 946, 1957.
238. Walker, W.F., M.S.
Zileli, F.W. Reutter,
W.C. Shoemaker, F.D.
Moore
Factors influencing the
'resting' secretion of
the adrenal medulla.
Am. J. Physiol. 197:765,
1959.
239. Wearn, J.T.
The role of the Thesbian
vessels in the circulation
of the heart.
J. Exp. Med. 47, 293, 1928.
241. Wearn, J.T.
Morphological and function-
al alterations of the coro-
nary circulation.
Harvey Lectures, pp. 248-
270, 1939-40.
242. Wegria, R.
Pharmacology of the coro-
nary circulation.
Pharmacological Reviews
3:197, 1951.
243. West, J.W., S.V.
Guzman
Coronary dilatation and
constriction visualized
by selective arteriography.
Circ. 18:798, Circ. Res.
7:527, 1959.
244. West, J.W., S.V.
Guzman, S. Bellet
Cardiac effects of intra-
coronary arterial injec-
tions of nicotine.
Circ. Research 6, 389,
1958.

245. West, J.W., T. Kobayshi,
S.V. Guzman Coronary artery catheteri-
zation in the intact dog.
Circ. Research 6, 383,
1958.
246. Widran, J. The dissection of the
atrioventricular node
bundle and bundle branches
in the human heart.
Circ. 4:863, 1951.
248. Wiggers, C.J. The functional importance
of coronary collaterals.
Circ. 5:609-15, 1952.
249. Wiggers, C.J. The interplay of coronary
vascular resistance and
myocardial compression in
regulating coronary flow.
Circ. Res. 2:27, 1954.
250. Wiggers, C.J., F.S.
Cotton Studies on the coronary
circulation. II. The
systolic and diastolic
flow through the coronary
vessels.
Am. J. Physiol. 106:597,
1933.
251. Winbury, M.M., P.M.
Michiels, W.E.
Hambourger, W.J.
Stockfish, D.L. Cook Coronary dilator action. I.
Quantitative assay in the
intact dog.
J. Pharmacol. and exp.
Therap. 99:343, 1950.
252. Winder, C.V., R.W.
Thomas, D. Kamm Relative experimental
coronary vasodilator poten-
cies of papaverine and its
ethyl analogue Ethaverine.
(Diquinaol, Perparin).
J. Pharmacol. and exp.
Therap. 100:482, 1950.
253. Wolff, A.L. (Company) Data on Doppler Ultra-
sonic Flowmeter Systems
in Reflections No. 2,
Allan L. Wolff Company, San
Marino, Cal. May, 1966.

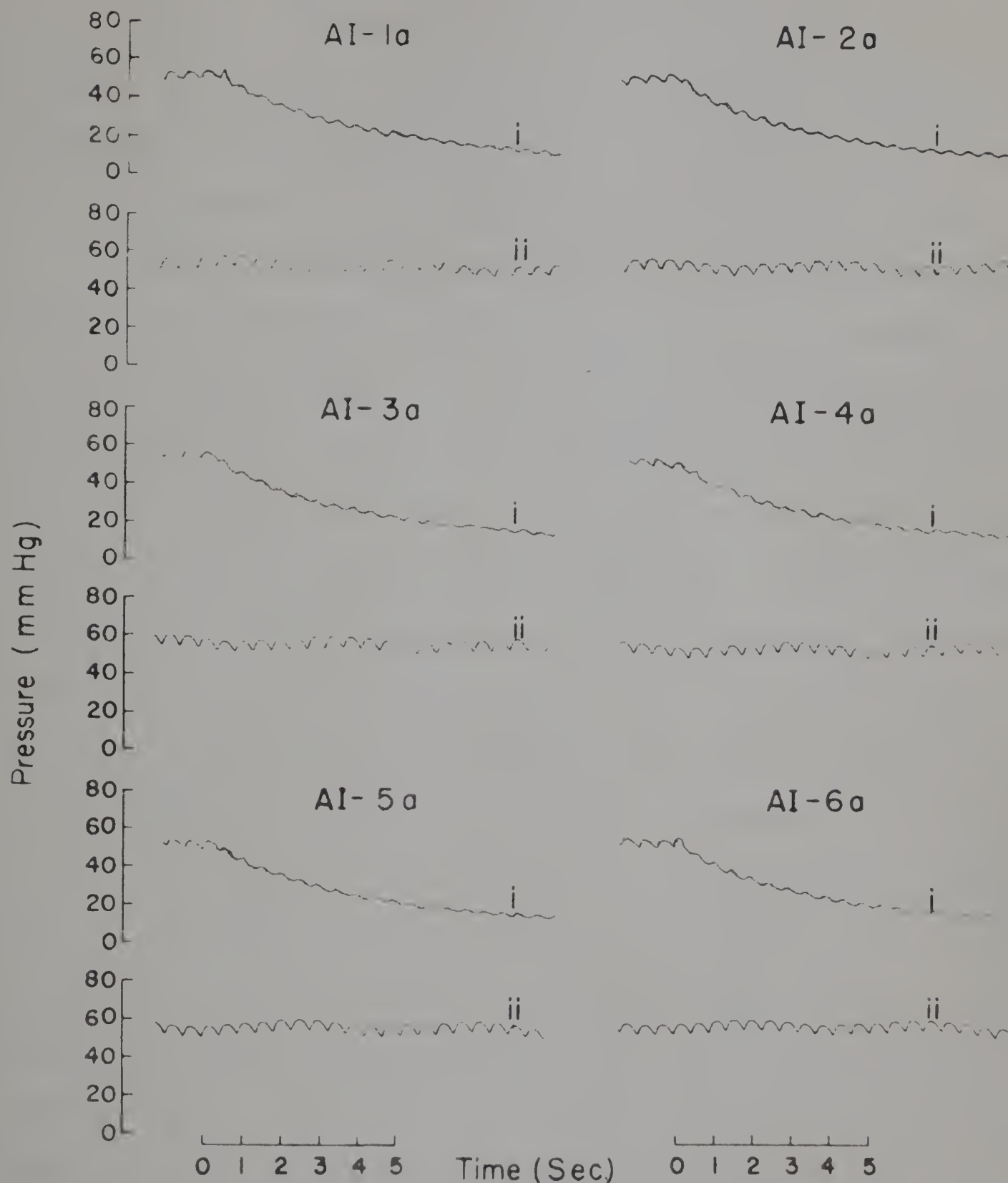
254. Woods, J.D. Relative ischemia in the hypertrophied heart. Lancet, I:696, 1961.
255. Zierler, K.L. Circulation times and the theory of indicator-dilution methods for determining blood flow and volume. Handbook of Physiology Washington, D.C., American Physiological Society, Sec. 2, Vol. 1, pp. 585-615, 1962.

APPENDIX I

1. JUSTIFICATION OF THE ASSUMPTION THAT THE FOUR PRESSURE SAMPLES TAKEN AT TIMES 0, 0.5, 1.0, AND 1.5 SECONDS FROM THE MANOMETRIC PERFUSION APPARATUS DURING THE PRESSURE 'DIE-AWAY' ARE SUFFICIENT TO CHARACTERIZE THE ENTIRE NATURE OF THE 'DIE-AWAY' CURVE AND THAT THE CURVE IS EXPONENTIAL

Figure M-4 illustrates the appearance of a family of 'die-away' curves from rigid tube perfusion systems analogous to that depicted in Figure M-3. That pressure decline in such a system of rigid tubes has the characteristic $P_t = P_0 \cdot e^{-at}$ (where: P_t = pressure at time t secs.; P_0 = initial pressure; and, $-a$ = a constant of exponential

Figures AI-1a - AI-6a



i Actual Pressure "Die-Aways" from Manometric
Perfusion Apparatus on a Live Dog

ii Aortic Blood Pressure

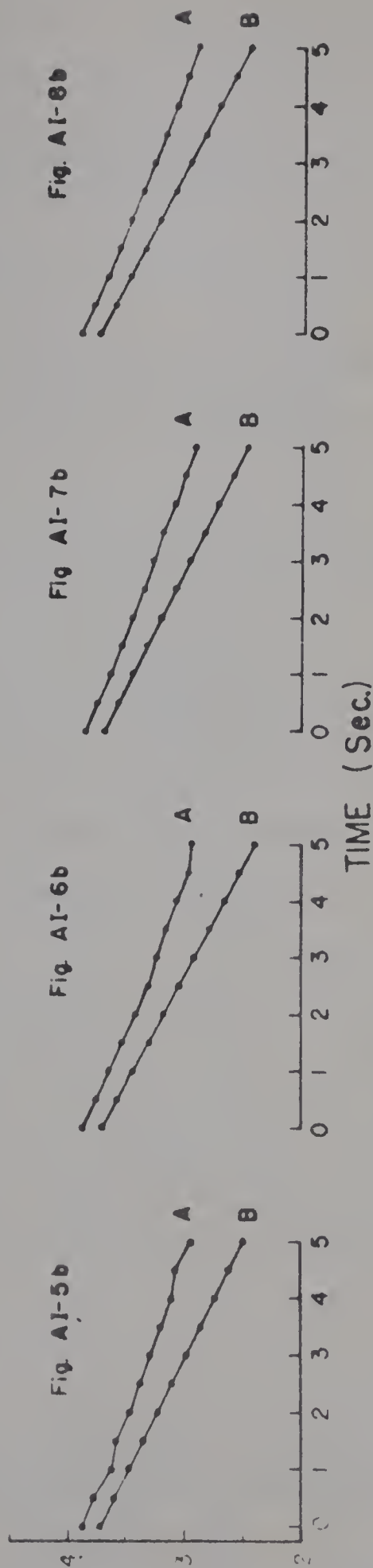
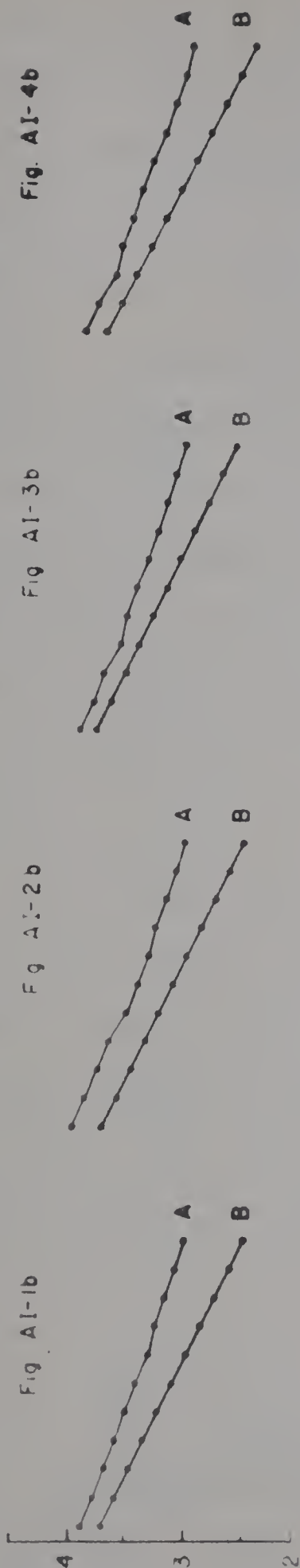
For full explanation see text, pp. 120, paragraph 2.

decay) has been demonstrated in "Flow-Pressure Relations in Rigid Tube Perfusion Systems" (of the Methods section of this thesis).

It can be demonstrated that the same characteristic, namely, $P_t = P_0 \cdot e^{-at}$ holds true for pressure decline curves produced by the manometric perfusion apparatus when connected to an animal in the appropriate way (see Fig. M-1).

Figures AI-1a to AI-6a (see also Appendix IV, Figs. AI-7a to AI-30a) are curves derived from the manometric perfusion apparatus connected to the left descending coronary artery of a living dog (anesthetic - sodium pentobarbital 30 mg/kg). If these curves are exponential decay curves of the character argued here then a semi-log plot of pressure versus time will produce a straight line of slope equal to "a" in the equation $P_t = P_0 \cdot e^{-at}$. Figs. AI-1b to AI-8b (see also Appendix IV, Figs. AI-9b to AI-30b) are such plots. (Table AI-2 is the pressures and Table AI-3 is the natural logarithms of the pressures in Table AI-2.) The upper curves (the curves labelled "A") in Figs. AI-1b to AI-30b are semi-log plots of the absolute gauge pressures versus time obtained from Figs. AI-1a to AI-30a respectively. These are clearly not straight line graphs. However, when the peripheral coronary pressure (p.c.p.) which is the pressure the system eventually dies away to, not zero, is subtracted from each pressure point in the "A" curves of Figs. AI-1b to AI-30b the result is a straight

FIGURES AI-1b - AI-8b



Pressure "Die-Aways" From Manometric Perfusion Apparatus

A. Pressure ($\text{Log}_e(\text{mm Hg})$) vrs. time

B. Pressure minus P.C.P. ($\text{Log}_e(\text{mm Hg})$) vrs. time

For full explanation see text, pp. 120, paragraph 2.

line of precisely slope equal to "a" when the data is fitted to the equation $P_t = P_0 \cdot e^{-at}$. The "B" curves in Figs. AI-1b to AI-30b are such semi-log plots of the pressures in the "A" curves with their corresponding p.c.p.'s subtracted from them.

The columns 3 and 5 of Table AI-3 are squares of correlation coefficients relating, the actual pressure (die-aways minus p.c.p.'s) with logarithms taken, to the ideal straight line of the same slope with no scatter of data points. A correlation coefficient squared of 0.94 indicates that with 95% confidence the die away was a single exponential. The correlation coefficient which appears squared in Table AI-3, column 3, was derived as follows: (the method is exactly similar for column 5 but 11 pressure samples were used) four pressure samples, P_1, P_2, P_3, P_4 are taken at times t_1, t_2, t_3, t_4 respectively. P_t (P_t = peripheral coronary pressure) is known. P'_1, P'_2, P'_3, P'_4 are transformed by subtraction of P_t and taking of natural logarithms to $P_{t_1}, P_{t_2}, P_{t_3}, P_{t_4}$, where $P_{t_i} = \ln (P'_i - P_t)$ then the correlation coefficient, r , is given by:

$$r = \frac{\sum_{i=1}^4 (P_{t_i} - \bar{P}_t)(t_i - \bar{t})}{\sqrt{\sum_{i=1}^4 (P_{t_i} - \bar{P}_t)^2 \cdot \sum_{i=1}^4 (t_i - \bar{t})^2}}$$

TABLE AI-1

PRESSURES FROM FIGURES AI-1aA TO AI-30aA AT TIMES
 0.0, 0.5 SEC., 1.0 SEC., 1.5 SEC., 2.0 SEC., 2.5
 SEC., 3.0 SEC., 3.5 SEC., 4.0 SEC., 4.5 SEC., AND
 5.0 SEC.

	Fig. AI-1aA	Fig. AI-2aA	Fig. AI-3aA	Fig. AI-4aA	Fig. AI-5aA	Fig. AI-6aA	Fig. AI-7aA	Fig. AI-8aA	Fig. AI-9aA
P ₀	49.00	53.00	50.00	48.00	49.00	48.00	48.00	51.00	51.00
P _{0.5}	44.30	47.40	45.20	43.20	44.10	42.90	43.30	45.60	45.50
P ₁	40.10	42.50	40.90	38.90	39.70	38.50	39.10	40.90	40.70
P _{1.5}	36.40	38.30	37.00	35.20	35.80	34.60	35.40	36.80	36.60
P ₂	33.10	34.50	33.60	31.90	32.40	31.20	32.10	33.20	32.90
P _{2.5}	30.20	31.20	30.60	29.00	29.40	28.20	29.20	30.00	29.70
P ₃	27.60	28.40	28.00	26.40	26.80	25.60	26.60	27.20	27.00
P _{3.5}	25.30	25.80	25.60	24.20	24.50	23.30	24.30	24.70	24.60
P ₄	23.30	23.60	23.50	22.20	22.40	21.30	22.30	22.60	22.40
P _{4.5}	21.60	21.70	21.70	20.50	20.60	19.50	20.60	20.70	20.60
P ₅	20.00	20.00	20.00	19.00	19.00	18.00	19.00	19.00	19.00

TABLE AI-1 (cont.)

	Fig. AI-10aA	Fig. AI-11aA	Fig. AI-12aA	Fig. AI-13aA	Fig. AI-14aA	Fig. AI-15aA	Fig. AI-16aA	Fig. AI-17aA	Fig. AI-18aA
P ₀	53.00	47.00	51.00	51.00	49.00	45.00	49.00	51.00	49.00
P _{0.5}	46.70	41.70	45.20	45.20	43.20	40.10	43.20	44.80	43.20
P ₁	41.30	37.10	40.10	40.10	38.30	35.90	38.30	39.50	38.30
P _{1.5}	36.70	33.10	35.80	35.80	34.00	32.20	34.00	34.90	34.00
P ₂	32.70	29.70	32.00	32.00	30.40	29.00	30.40	31.00	30.40
P _{2.5}	29.20	26.70	28.70	28.70	27.20	26.20	27.20	27.70	27.20
P ₃	26.30	24.20	25.90	25.90	24.50	23.80	24.50	24.80	24.50
P _{3.5}	23.70	22.00	23.50	23.50	22.20	21.80	22.20	22.40	22.20
P ₄	21.50	20.10	21.40	21.40	20.20	19.90	20.20	20.30	20.20
P _{4.5}	19.60	18.40	19.60	19.60	18.50	18.40	18.50	18.50	18.50
P ₅	18.00	17.00	18.00	18.00	17.00	17.00	17.00	17.00	17.00

TABLE AI-1 (cont.)

	Fig. AI-19aA	Fig. AI-20aA	Fig. AI-21aA	Fig. AI-22aA	Fig. AI-23aA	Fig. AI-24aA	Fig. AI-25aA	Fig. AI-26aA	Fig. AI-27aA
P ₀	47.00	50.00	80.00	82.00	90.00	92.00	86.00	94.00	86.00
P _{0.5}	41.70	44.00	74.20	74.30	81.00	84.00	77.50	85.10	78.10
P ₁	37.10	38.90	68.90	67.50	73.10	76.80	70.10	77.20	71.10
P _{1.5}	33.10	34.50	64.10	61.50	66.10	70.40	63.40	70.10	64.80
P ₂	29.70	30.70	59.70	56.10	59.90	64.60	57.60	63.80	59.20
P _{2.5}	26.70	27.40	55.60	51.20	54.40	59.30	52.30	58.20	54.10
P ₃	24.20	24.70	51.90	47.00	49.50	54.60	47.70	53.20	49.70
P _{3.5}	22.00	22.30	48.50	43.10	45.20	50.40	43.70	48.70	45.60
P ₄	20.10	20.20	45.40	39.70	41.40	46.50	40.00	44.70	42.10
P _{4.5}	18.40	18.50	42.60	36.70	38.00	43.10	36.80	41.20	38.90
P ₅	17.00	17.00	40.00	34.00	35.00	40.00	34.00	38.00	36.00

TABLE AI-1 (cont.)

	Fig. AI-28aA	Fig. AI-29aA	Fig. AI-30aA
P ₀	78.00	76.00	72.00
P _{0.5}	69.60	67.00	63.10
P ₁	62.30	59.20	55.50
P _{1.5}	55.90	52.60	49.00
P ₂	50.40	46.80	43.50
P _{2.5}	45.50	41.90	38.80
P ₃	41.20	37.70	34.80
P _{3.5}	37.50	34.10	31.40
P ₄	34.30	31.00	28.60
P _{4.5}	31.50	28.30	26.10
P ₅	29.00	26.00	24.00

In order to justify that only four pressure samples (taken at one-half second intervals, including time zero, from curves such as those seen in Fig. M-2 and Figs. AI-1a to AI-30a) are sufficient to characterize the entire curve, it need only be shown that the value of "a", in the equation $P_t = P_0 \cdot e^{-at}$ when determined from the four said pressure samples, is in very close agreement with the value of "a" obtained when a large number of pressure samples are used. Since the data points all fall along a straight line in a semi-log plot of pressure versus time this condition has been satisfied. Table AI-3 is a comparison of values of "a" determined from the four said samples over 1.5 seconds and the corresponding values for "a" when eleven samples were taken over 5 seconds. The difference is not significant.

Since the characteristics of the die away curves obtained from live animals are precisely similar to those obtained from rigid tube perfusion systems, the same method of determining flow as has been described for rigid tube systems (see Methods, referred to above) is valid.

A. Analysis of Data in Table AI-3

The columns two and four of Table AI-3 are considered to be vectors giving the same number of observations on an independent variable x ("a" in $P_t = P_0 \cdot e^{-at}$ derived from 11 pressure samples in 5.0 seconds) and a dependent variable

TABLE AI-2

LOG_e OF PRESSURES IN TABLE AI-1
PLOTTED IN FIG. AI-1bi TO AI-30bi

	Fig. AI-1bi	Fig. AI-2bi	Fig. AI-3bi	Fig. AI-4bi	Fig. AI-5bi	Fig. AI-6bi	Fig. AI-7bi	Fig. AI-8bi	Fig. AI-9bi
P ₀	3.89	3.97	3.91	3.87	3.89	3.87	3.87	3.98	3.93
P _{0.5}	3.79	3.86	3.81	3.77	3.79	3.76	3.77	3.82	3.82
P ₁	3.69	3.75	3.71	3.66	3.68	3.65	3.67	3.71	3.71
P _{1.5}	3.59	3.65	3.61	3.56	3.58	3.54	3.57	3.61	3.60
P ₂	3.50	3.54	3.51	3.46	3.48	3.44	3.47	3.50	3.50
P _{2.5}	3.41	3.44	3.42	3.37	3.38	3.34	3.37	3.40	3.39
P ₃	3.32	3.35	3.33	3.27	3.29	3.24	3.28	3.30	3.30
P _{3.5}	3.23	3.25	3.24	3.19	3.20	3.15	3.19	3.21	3.20
P ₄	3.15	3.16	3.16	3.10	3.11	3.06	3.10	3.12	3.11
P _{4.5}	3.07	3.08	3.08	3.02	3.03	2.97	3.03	3.03	3.03
P ₅	3.00	3.00	3.00	2.94	2.94	2.89	2.94	2.94	2.94

TABLE AI-2 (cont.)

	Fig. AI-10bi	Fig. AI-11bi	Fig. AI-12bi	Fig. AI-13bi	Fig. AI-14bi	Fig. AI-15bi	Fig. AI-16bi	Fig. AI-17bi	Fig. AI-18bi
P ₀	3.97	3.85	3.93	3.93	3.89	3.80	3.89	3.93	3.89
P _{0.5}	3.84	3.73	3.81	3.81	3.77	3.69	3.77	3.80	3.77
P ₁	3.72	3.61	3.69	3.69	3.65	3.58	3.65	3.68	3.65
P _{1.5}	3.60	3.50	3.58	3.58	3.53	3.47	3.53	3.55	3.53
P ₂	3.49	3.39	3.47	3.47	3.41	3.37	3.41	3.43	3.41
P _{2.5}	3.37	3.28	3.36	3.36	3.30	3.27	3.30	3.32	3.30
P ₃	3.27	3.19	3.25	3.25	3.20	3.17	3.10	3.21	3.10
P _{3.5}	3.17	3.09	3.16	3.16	3.10	3.08	3.10	3.10	3.10
P ₄	3.07	3.00	3.06	3.06	3.01	2.99	3.01	3.01	3.00
P _{4.5}	2.98	2.91	2.98	2.98	2.92	2.91	2.92	2.92	2.92
P ₅	2.89	2.83	2.89	2.89	2.83	2.83	2.83	2.83	2.83

TABLE AI-2 (cont.)

	Fig. AI-19bi	Fig. AI-20bi	Fig. AI-21bi	Fig. AI-22bi	Fig. AI-23bi	Fig. AI-24bi	Fig. AI-25bi	Fig. AI-26bi	Fig. AI-27bi
P ₀	3.85	3.91	4.38	4.41	4.50	4.52	4.45	4.54	4.45
P _{0.5}	3.73	3.78	4.31	4.31	4.39	4.43	4.35	4.44	4.35
P ₁	3.61	3.66	4.23	4.21	4.29	4.34	4.25	4.35	4.26
P _{1.5}	3.40	3.54	4.16	4.12	4.19	4.25	4.15	4.25	4.17
P ₂	3.39	3.42	4.08	4.03	4.09	4.17	4.05	4.16	4.08
P _{2.5}	3.28	3.31	3.02	3.94	3.97	4.08	3.96	4.06	3.99
P ₃	3.19	3.21	3.95	3.85	3.90	4.00	3.86	3.97	3.90
P _{3.5}	3.09	3.10	3.88	3.76	3.81	3.92	3.78	3.89	3.82
P ₄	3.00	3.00	3.82	3.68	3.72	3.84	3.69	3.80	3.74
P _{4.5}	2.91	2.92	3.75	3.60	3.64	3.76	3.61	3.71	3.66
P ₅	2.83	2.83	3.69	3.53	3.56	3.69	3.53	3.64	3.58

TABLE AI-2 (cont.)

	Fig. AI-28bi	Fig. AI-29bi	Fig. AI-30bi
P ₀	4.35	4.33	4.27
P _{0.5}	4.24	4.20	4.14
P ₁	4.13	4.08	4.02
P _{1.5}	4.02	3.96	3.89
P ₂	3.92	3.85	3.77
P _{2.5}	3.82	3.74	3.66
P ₃	3.71	3.63	3.55
P _{3.5}	3.62	3.63	3.55
P ₄	3.54	3.43	3.35
P _{4.5}	3.45	3.34	3.26
P ₅	3.37	3.26	3.18

y ("a" in $P_t = P_0 \cdot e^{-at}$ derived from 4 pressure samples in 1.5 seconds). The straight line of the form $Y = A+B \times X$ was fitted to these data by the method of least squares with the following results:

mean of x = -0.2680489391

standard deviation of x = 0.0347151056

mean of y = -0.2679042278

standard deviation of y = 0.0347016537

A = -0.0000035583

B = 0.9994468564

standard error of B = 0.0034389727

T value = 290.6236637813

standard error of estimate = 0.0006429041

correlation coefficient = 0.9998342864

square of correlation coefficient = 0.9996686003

The conclusion reached by this sort of analysis is simply that the observations in x ("a" in $P_t = P_0 \cdot e^{-at}$ derived from 11 pressure samples) do not differ significantly from the observations in y (the corresponding values of "a" in $P_t = P_0 \cdot e^{-at}$ derived from only 4 pressure samples). In fact, the probability of this similarity occurring by chance is $P < 0.0001$ from $n = 28$ (degrees of freedom).

TABLE AI-3

COMPARISON OF VALUES OBTAINED FOR 'a' IN THE

EQUATION $P_t = P_0 \cdot e^{-at}$. DATA DERIVED FROM

CURVES IN FIGURES AI-1a TO AI-30a

1	2	3	4	5
Data from fig.	a, derived from 11 pressure samples in 5.0 secs.	square of corr. coef. relating column 2 to ideal	a, derived from 4 pressure samples in 1.5 secs.	square of corr. coef. relating column 4 to ideal
AI-1a	-0.2460369464	0.9999852573	-0.2449020951	0.9999963745
AI-2a	-0.2643787765	0.9999913174	-0.2638701648	0.9999678153
AI-3a	-0.2391605483	0.9999845692	-0.2398857407	0.9999462982
AI-4a	-0.2586667741	0.9999919074	-0.2574554682	0.999983376
AI-5a	-0.2505898637	0.9999919715	-0.251624917	0.9999712719
AI-6a	-0.2633471815	0.9999951642	-0.2636037263	0.9999916548
AI-7a	-0.2460369464	0.9999852573	-0.2449020951	0.9999963745

TABLE AI-3 (cont.)

AI-8a	-0.2594588602	0.9999931682	-0.2597761967	0.9999877612
AI-9a	-0.2726905122	0.9999868514	-0.2720692097	0.9999722142
AI-10a	-0.3009946024	0.9999934023	-0.2999156608	0.9999890813
AI-11a	-0.2932177034	0.9999911295	-0.2937682126	0.9999923571
AI-12a	-0.2915770699	0.9999938476	-0.2911890032	0.9999791936
AI-13a	-0.2915770699	0.9999938476	-0.2911890032	0.9999791936
AI-14a	-0.3029993774	0.9999958641	-0.3032649912	0.9999848681
AI-15a	-0.2825602367	0.9999786129	-0.282785036	0.9999923678
AI-16a	-0.3029993774	0.9999958641	-0.3032649912	0.9999848681
AI-17a	-0.3131171706	0.9999962647	-0.3125463573	0.9999878089
AI-18a	-0.3029993774	0.9999958641	-0.3032649912	0.9999848681
AI-19a	-0.2932177034	0.9999911295	-0.2937682126	0.9999923571
AI-20a	-0.3083543131	0.9999895231	-0.3068674821	0.9999972575
AI-21a	-0.1774984493	0.9999971342	-0.1776175856	0.9999924878
AI-22a	-0.2315161803	0.9999949506	-0.2310292245	0.9999830703
AI-23a	-0.2441092307	0.9999986492	-0.2438437122	0.9999963239

TABLE AI-3 (cont.)

AI-24a	-0.2099520252	0.9999969575	-0.20989855	0.9999897638
AI-25a	-0.2427495023	0.9999940504	-0.2426330482	0.9999836257
AI-26a	-0.2296679102	0.9999985047	-0.2296059296	0.9999977957
AI-27a	-0.2250735902	0.9999944428	-0.224919906	0.9999974816
AI-28a	-0.271186456	0.9999957713	-0.2717477513	0.9999992309
AI-29a	-0.3038758751	0.9999974202	-0.3036568686	0.9999921999
AI-30a	-0.3218585417	0.9999936213	-0.3222607016	0.9999967813

APPENDIX II

1. APL/360 COMPUTER PROGRAM OPERATION FOR MANOMETRIC PERFUSION PRESSURE, FLOW, AND RESISTANCE MEASUREMENT

General

Figure AII-1 illustrates the principles of the manometric perfusion apparatus in operation for measurement of blood flow in the left descending Coronary artery. Figure AII-2 is a typical analogue record of a single flow measurement. A single experimental or control exercise consisted of large numbers of similar measurements, except that readings of transmitted pressure, which involved total occlusion - which, however brief, might

produce artefact from reactive hyperaemia - were limited to not more than once every 5 mins.

Data for input to the computer was manually converted from the analogue record to digital format suitable for the program. The data from a single measurement was construed as a single row of a two dimensional six column matrix such that: the first column was the peripheral coronary pressure in mm Hg. (determined from Fig. AII-2A at time 4.5 sec.); the second column was Aortic systemic pressure in mm Hg. (determined from Fig. AII-2B at time 0); the third column was the initial manometric perfusion pressure (determined from Fig. AII-2A at time 0); the fourth column was manometric perfusion pressure sample two (determined from Fig. AII-2A at time 0.5 sec.); the fifth column was manometric perfusion pressure sample three (determined from Fig. AII-2A at time 1.0 sec.); the sixth column was manometric perfusion pressure sample three (determined from Fig. AII-2A at time 1.5 sec.). The data from AII-2 appeared after manual analogue - digital conversion in six column matrix format as follows:

P.C.P.	A.B.P.	t_0	$t_{0.5}$	$t_{1.0}$	$t_{1.5}$
24	89	87	82	74	72

The result, outputted from the computer appeared after computation in seven column matrix format as follows:

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
24	89	6.64	10.60	6.70	3.90	0.960

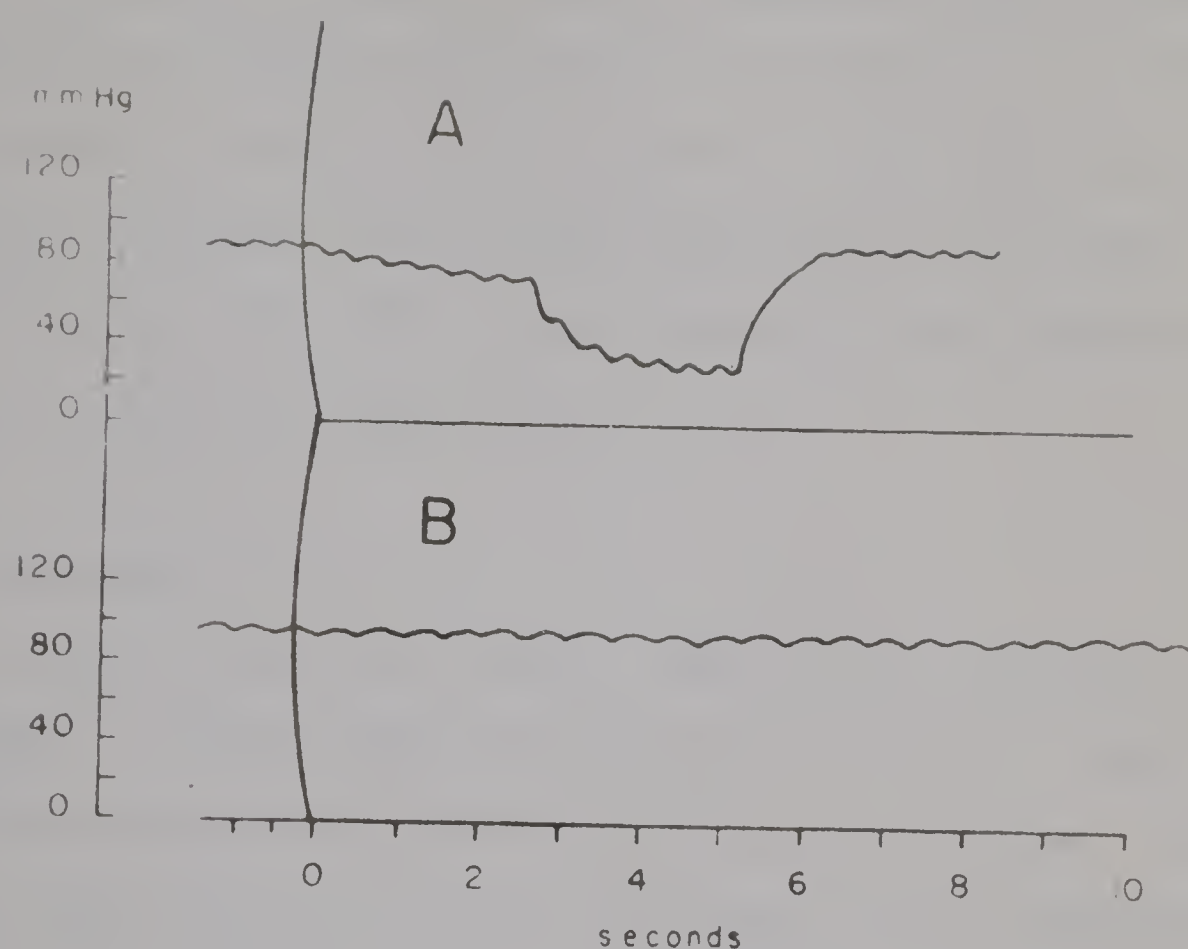


Fig. AII-2

Analogue record produced using manometric perfusion apparatus.

- A. Pressure decline from time 0 to time 2.5 seconds, time 2.5 to 4.5 seconds - peripheral coronary pressure.
- B. Aortic systemic blood pressure.

where the first column was peripheral coronary pressure; the second column was aortic systemic pressure; the third column was flow in ml/min; the fourth, fifth, and sixth columns were total left descendens vascular bed resistance, left descendens vessel element resistance and peripheral coronary resistance respectively in $\text{Newton} \cdot \text{sec} \cdot \text{cm}^{-5}$; and the seventh column was the square of the correlation coefficient relating the pressure decline to the ideal curve of the form $P_t = P_0 \cdot e^{-at}$. (See Appendix I for explanation of the correlation coefficient.)

A. Program

Figure AII-3 is a "hard" copy of the computer APL/360 program. Figures AII-4 and AII-5 are similar "hard" copies of the sub-routines which appear in the program. The program CORON (Fig. AII-3) was designed to be preceded by a vector 'T' which was the times at which the manometric perfusion pressure samples were taken (i.e. $T = 0.0, 0.5, 1.0, 1.5$ seconds) and anteceded by a six column matrix 'M' in which each row is a set of data from one measurement. There may be as many rows in the matrix 'M' as there were measurements in a particular experimental or control exercise. Table AII-1 is such an input matrix (an actual manual digitally converted analogue). Output data is formatted as a seven column matrix of length equal to the length (number of rows) of the input matrix 'M'. Output data is assigned

▽ R←T CORON M;C;D;E;F;G;H;I

- [1] F←((ρM)[1]),7)ρ0
- [2] C←1
- [3] LAP:D←P MP⊕(E←M[C;2+14])-M[C;1]
- [4] G←M[C;2]
- [5] H←2 RND 0.53×(G-M[C;1])×-D[4;1]
- [6] I←G×1330÷H÷60÷10×5
- [7] F[C;]←(M[C;1]),G,H,(3 RND I),(3 RND (G-M[C;1])×
1330÷H÷60÷10×5),(3 RND M[C;1]×1330÷H÷60÷10×5),
3 RND D[5;3]
- [8] C←C+1
- [9] →(C≤(ρM)[1])/LAP
- [10] R←F

▽

Fig. AII-3

Pressure, flow resistance function. Computer (APL/360) program for manometric perfusion data.

▽ SR [] ▽

▽ P←A SR Y;N;MX;SX;MY;SY;B1;B0;R;RSQ;TV;SE;A;B

[1] $SX \leftarrow ((A \leftarrow + / (X - MX \leftarrow (+ / X) \div N) * 2) \div (N \leftarrow (p X)) - 1) *$

0.5

[2] $SY \leftarrow ((B \leftarrow + / (Y - MY \leftarrow (+ / Y) \div N) * 2) \div N - 1) *$

0.5

[3] $B0 \leftarrow MY - MX \times B1 \leftarrow (+ / (X - MX) \times (Y - MY)) \div A$

[4] $SE \leftarrow ((B \times 1 - RSQ \leftarrow (R \leftarrow B1 \times SX \div SY) * 2) \div N - 2) *$

0.5

[5] $TV \leftarrow B1 \div SE1 \leftarrow (SY \div SX) \div ((N - 2) \div (1 - RSQ)) *$

0.5

[6] $T \leftarrow (5 \ 3) p MX, SX, 0, MY, SY, 0, B0, \ 0 \ 0, B1, SE1, TV, SE, P, RSQ$

▽

Fig. AII-4

Simple regression function. Sub-routine APL/360 program for manometric perfusion data.


```

▽ RND [ ] ▽
▽ P←N RND X
[1] P←(10*N)×[0.5+X×10*N]
▽

```

Fig. AII-5

Rounding function sub-routine APL/360 program for manometric perfusion data.

to matrix 'R'. Each row of data is the result corresponding to the same row of input data in 'M'. Table AII-2 is such an output matrix (an actual computer output record corresponding to the input matrix 'M' depicted in Table AII-1). Each row of input data in 'M' is treated individually in the program by incremental steps. CORON ((1)) (Fig. AII-3) assigns the dimensions of the output matrix 'R' (called F). CORON ((2)) stipulates the row number of the input matrix 'M' to be operated on initially as the working variable 'C'. CORON ((3)) breaks into the sub-routine SR (Fig. AII-4) which considers 'T' (the time vector 0.0, 0.5, 1.0, 1.5 sec.) to be an independent variable and the natural logarithm of the pressure vector 'E' ($P_0, P_{0.5}, P_{1.0}, P_{1.5}$) to be a dependent variable to which the line of the form $A+B \times X$ is fitted by the method of least squares. The result of the sub-routine 'SR' is then stored in the variable 'D'. The data in 'D' is the same as that outlined in Appendix I, Section A, Analysis of Data in Table AII-3. CORON ((5)) stores in the variable 'H' the product of the manometer constant (see Methods, Flow-Pressure Relations in Rigid Tube Perfusion Systems) the perfusion pressure (aortic systemic pressure - peripheral coronary pressure), and the slope of the line fitted by the sub-routine 'SR' which is equal to 'a' in the description $P_t = P_0 \cdot e^{-at}$. This product is flow in ml/min (see Methods, Flow Measurement by Manometric Perfusion). The sub-routine 'RND' (Fig. AII-5) where ever it appears

simply serves to round down numbers from 10 places of decimals to the number of decimals preceeding the statement 'RND' (i.e. 2 'RND' in CORON ((5))). CORON ((6)) converts the pressure drop across the vascular bed of the left descendens into units of $\text{Newt}.\text{sec}.\text{cm}^{-5}$. CORON ((7)) converts the pressure drop from aortic to peripheral coronary pressure and the pressure drop from peripheral coronary to central venous pressure to units of $\text{Newt}.\text{sec}.\text{cm}^{-5}$ and arranges all the output data into a single row of the matrix 'R' (Table AII-2). CORON ((8)) increments the value of the running variable C to 1 plus whatever it was. CORON ((9)) tests the value of C to be sure it is not larger than the number of rows in the input matrix 'M' and then branches to CORON ((3)) where the whole process is repeated with the subsequent row of data from the input matrix 'M' (Table AII-1). When this has been done for every row of 'M', then CORON ((10)) prints the matrix 'R' (Table AII-2).

TABLE AII-1

Weight: 12 Kg. Age: 3 Yrs. Sex: ♂ Date: May 9, 1968

Series: P.C.P. and Network Pressure

P (pcp)	P (A)	P (O)	P (1)	P (2)	P (3)
26	100	99	89	84	79
26	108	100	92	87	82
28	108	98	91	86	81
				Occlusion Off	
27	102	73	63	57	53
26	100	78	68	61	56
27	104	84	72	63	58
27	106	82	71	65	59
27	104	82	70	65	60
27	104	82	72	65	60
28	106	88	74	68	61
28	106	82	73	66	62
28	106	86	76	70	64
28	106	87	78	69	63
28	108	91	80	75	70
28	106	96	85	78	72
28	108	94	85	80	75
28	110	94	86	80	76
28	104	93	85	80	75
28	110	100	90	85	80
30	108	96	88	80	75
28	106	96	88	80	75
28	106	94	86	80	74
28	106	97	88	82	76
28	104	98	88	80	74
				Nembutal 1 cc.	
28	108	96	89	83	77
28	111	100	89	82	76
28	110	95	86	80	75
28	110	100	90	82	76
				Hemorrhage	
24	85	75	68	62	58
22	88	81	71	66	61
22	86	75	69	65	61
22	88	77	70	65	61
22	88	78	71	67	63
				Hemorrhage	
17	65	56	52	49	46
16	66	55	51	49	46
17	66	58	53	50	47
17	66	57	52	49	47

TABLE AII-1 (cont.)

P (pcp)	P (A)	P (O)	P (1)	P (2)	P (3)
18	67	59	55	52	50
				Hemorrhage	
14	50	42	40	38	36
14	46	40	37	35	33
14	45	39	36	34	32
14	45	38	35	33	32
14	46	41	38	36	34
10	32	26	24	23	22
10	27	23	21	20	19
12	30	23	22	21	20
10	26	22	21	20	19
11	28	22	21	20	19
				Hemorrhage	
9	20	15	13	12	11
9	18	14	12	11	10
10	18	14	13	12	11
9	14	11	10	9	8
8	13	10	9	8	8

TABLE AII-2

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
26.000	100.000	8.180	9.756	7.219	2.536	0.981
26.000	108.000	7.950	10.841	8.231	2.610	0.993
28.000	108.000	7.780	11.078	8.206	2.872	0.998
27.000	102.000	15.060	5.405	3.974	1.431	0.986
26.000	100.000	14.370	5.553	4.109	1.444	0.995
27.000	104.000	16.730	4.961	3.673	1.288	0.990
27.000	106.000	14.830	5.704	4.251	1.453	0.993
27.000	104.000	13.520	6.138	4.545	1.594	0.973
27.000	104.000	13.890	5.975	4.424	1.551	0.994
28.000	106.000	15.980	5.293	3.895	1.398	0.985
28.000	106.000	12.870	6.572	4.836	1.736	0.989
28.000	106.000	12.930	6.542	4.814	1.728	0.995
28.000	106.000	14.590	5.798	4.266	1.531	0.998
28.000	108.000	11.170	7.716	5.715	2.000	0.976
28.000	106.000	11.880	7.120	5.239	1.881	0.993
28.000	108.000	9.420	9.149	6.777	2.372	0.988
28.000	110.000	9.250	9.490	7.074	2.416	0.989
28.000	104.000	8.580	9.673	7.069	2.604	0.994
28.000	110.000	9.220	9.521	7.097	2.423	0.981
30.000	108.000	10.730	8.032	5.801	2.231	0.996
28.000	106.000	10.340	8.181	6.020	2.161	0.996
28.000	106.000	9.860	8.579	6.313	2.266	0.999
28.000	106.000	9.870	8.570	6.306	2.264	0.997
28.000	104.000	11.300	7.344	5.367	1.977	0.997

TABLE AII-2 (cont.)

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
28.000	108.000	9.210	9.358	6.932	2.426	1.000
28.000	111.000	11.770	7.526	5.627	1.898	0.993
28.000	110.000	10.190	8.614	6.422	2.193	0.993
28.000	110.000	11.770	7.458	5.560	1.898	0.997
24.000	85.000	8.810	7.699	5.525	2.174	0.996
22.000	88.000	9.440	7.439	5.579	1.860	0.984
22.000	86.000	6.850	10.019	7.456	2.563	0.996
22.000	88.000	7.980	8.800	6.600	2.200	0.994
22.000	88.000	7.140	9.835	7.376	2.459	0.989
17.000	65.000	4.980	10.416	7.692	2.724	0.999
16.000	66.000	4.480	11.756	8.906	2.850	0.989
17.000	66.000	5.320	9.900	7.350	2.550	0.992
17.000	66.000	4.950	10.640	7.899	2.741	0.974
18.000	67.000	4.300	12.434	9.093	3.340	0.987
14.000	50.000	3.070	12.997	9.358	3.639	0.999
14.000	46.000	3.500	10.488	7.296	3.192	0.996
14.000	45.000	3.550	10.115	6.968	3.147	0.996
14.000	45.000	3.160	11.364	7.828	3.535	0.967
14.000	46.000	3.350	10.958	7.623	3.335	0.996
10.000	32.000	2.190	11.660	8.016	3.644	0.979
10.000	27.000	2.160	9.975	6.281	3.694	0.982
12.000	30.000	2.020	11.851	7.111	4.741	0.998
10.000	26.000	1.630	12.729	7.833	4.896	0.998
11.000	28.000	1.910	11.698	7.103	4.596	0.998

TABLE AII-2 (cont.)

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
9.000	20.000	4.180	3.818	2.100	1.718	0.996
9.000	18.000	4.990	2.879	1.439	1.439	0.988
10.000	18.000	3.870	3.712	1.650	2.062	0.961
7.000	14.000	3.390	3.296	1.648	1.648	0.961
7.000	13.000	2.540	4.084	1.885	2.199	0.899

APPENDIX III

1. STATISTICAL APPENDIX:
APL/360 COMPUTER PROGRAMS AND TREATMENT USING THEM
FOR ANALYSIS OF CONTROL AND EXPERIMENTAL RESULTS.

The data in Results section Tables RC-1 to RC-7 (control data) and Tables RE-1 to RE-21 (experimental data) was treated as described in Methods¹ section of this thesis.

Fig. AIII-1A illustrates the computer program (APL/360) which was used to process the data representing a single infusion. The program "DO" operated in the form X DO Y

-
1. Methods, 5. Control (Saline) Infusions,
C. Analysis of Infusion Information.

▽ DO [] ▽

▽ P←X DO Y;A;B;C;D;E;F;G

[1] P←A←LIT(21 4 DFT X MCYC Y)

▽

A. APL/360 Program for statistics

▽ LIT [] ▽

▽ R←LIT X;A;B;C;D;E;F;G;H;I

[1] A←(ρX)[2]

[2] B←(28,A)ρ ' '

[3] B[1;35+128]←'PERIPHERAL CORONARY PRESSURE'

[4] B[5;38+121]←'AORTIC BLOOD PRESSURE'

[5] B[13;41+116]←'TOTAL RESISTANCE'

[6] B[17;37+125]←'VESSEL ELEMENT RESISTANCE'

[7] B[21;34+130]←'PERIPHERAL CORONARY RESISTANCE'

[8] B[9;36+126]←'LEFT DESCENDENS BLOOD FLOW'

[9] B[25;37+125]←'CORRELATION COEFFICIENT*2'

[10] B[1+13;]←X[13;]

[11] B[5+13;]←X[4+13;]

[12] B[9+13;]←X[8+13;]

[13] B[13+13;]←X[12+13;]

[14] B[17+13;]←X[16+13;]

[15] B[21+13;]←X[20+13;]

[16] B[25+13;]←X[24+13;]

[17] R←B

▽

B. APL/360 Literal heading sub-routine

Fig. AIII-1 (cont.)

```

[1]  V Z←W DFT X;D;E;F;G;H;I;J;K;L;Y
[2]  D←' 0123456789.'
[3]  →(V/W≠[W←,W+(H←0)×L←1<ρρX)/DFTERR+0×F←2
[4]  →(3 2 1 <ρρX)/(DFTERR+F←0), 2 3 +I26
[5]  →(ρρρX←((V/ 1 2 =ρW)Φ 1 2)Q(1,ρ,X)ρX)/2+I26
[6]  X←(0 1 1 /ρX)ρX
[7]  →((^/(ρW)≠ 1 2 , 2×E←1ρΦρX), 1≠ρW)/(DFTERR×F←1), 3+I26
[8]  I←1+[ /0, [10⊕|X+1>|X
[9]  W←(2+I+W+(W≠0)+v/, X<0), W
[10] →(V/2>-/[1]W←Q(E,2)ρW)/DFTERR+0×F←2
[11] Z←((K←1ρρX), +/W[1;])ρ',
[12] X←J-1|J←0.5+X×10*(ρX)ρW[2;]
[13] DFTLP:→(F<H←H+1)/DFTEND
[14] J←1+10|J-1|J←(|Y←X[;H])°.÷10*~1+Φ1I←W[1;H]
[15] J←(,J)×G←,Q(ΦρJ)ρ(,Q(J≠1)V.^(1I)°.≤1I-F+1), (K×1+F←W[2;H])ρ1
[16] →(^/0≤Y)/2+I26
[17] J[(I-+/(K,I)ρG)+I×~1+1K]←12×Y<0
[18] J←(K,I)ρJ
[19] →(0=F)/3+I26
[20] J←J[;(1Φ1G), (G←-/W[;H])+1F]
[21] J[;G]←11
[22] →DFTLP×ρρZ[;(+/W[1;1H-1])+1I]←D[1+J]
[23] DFTEND:→L/0
[24] →0×ρZ←,Z
[25] DFTERR:'DFT ',(3 6 ρ' RANK LENGTHDOMAIN')[F+1;],' PROBLEM.'

```

C. Formatting Sub-routine

Fig. AIII-1 (cont.)

```

[1]  ▽ R←A MCYC B;K;J;I
[2]  J←(ρA)[2]
[3]  R←((4×J),4)ρ0
[4]  K←1
[5]  R[(4×1+K)+13;]←((A[;K]>0)/A[;K])TTEST((B[;K]>0)/B[;K])
[6]  K←K+1
      →(K≤J)/4
      ▽

```

D. Cyclic program sub-routine

```

[1]  ▽ R←X1 TTEST X2;S;T;A;B;N1;N2;C
[2]  A←MVSD X1
[3]  B←MVSD X2
[4]  N1←ρX1
[5]  N2←ρX2
[6]  S←(((+/(X1-A[1;1])*2)+/(X2-B[1;1])*2)÷(N1-1)+N2-1)*0.5
[7]  T←((A[1;1]-B[1;1])÷S)×((N1×N2)÷N1+N2)*0.5
      R← 3 4 ρT,(N1+N2-2), 0 0 ,(4ρA),(4ρB)
      ▽

```

E. Determination of "T" value sub-routine

```

[1]  ▽ T←MVSD X;N;N;VAR;SD
[2]  SD←(VAR←(+/[1](X-(ρX)ρM←(+/[1]X)÷N)*2)÷(N←(ρX)[1])-1)*0.5
      T←Q(4,ρM,10)ρM,VAR,SD,(SD÷N*0.5)
      ▽

```

F. Mean, variance, standard deviation and standard error of the mean determination - sub-routine

where X was the matrix of pre-infusion data (i.e. Table RC-1, infusion number 1, pre-infusion data) and Y was the matrix of infusion data (i.e. Table RC-1, infusion number 1, infusion data). The only algorithm in "DO" refers directly or indirectly to all the sub-routines in the program.

The first sub-routine "LIT" (see Fig. AIII-1B) applies the section headers to the output print (hard copy) denoting the particular parameter of measurement under analysis. The parameters of measurement are peripheral coronary pressure (P.C.P.), aortic blood pressure (A.B.P.), left descendens blood flow (FLOW), total resistance (C.R.), vessel element resistance (C.V.R.), peripheral coronary resistance (P.C.R.).

The second sub-routine "DFT" (see Fig. AIII-1, C) was simply a formatting function which arranged the data in orderly fashion under the appropriate heading printed by "LIT".

The third sub-routine "MCYC" (see Fig. AIII-1, D) selected the corresponding columns of the input matrices (i.e. the peripheral coronary pressure columns of the pre-infusion data set and the infusion data set) and directed them cyclicly (first P.C.P., second A.B.P., third FLOW, etc.) into the fourth sub-routine "T-TEST" (see Fig. AIII-1, E) which performed Student's T-test for significance of means on the data in the print out and entered the T-value and number of degrees of freedom.

The fifth and final sub-routine "MVSD" (see Fig.

AIII-1, F) calculated the means, variances, standard deviations, and standard error of the means of each data set that was T-tested.

Table AIII-1 has the form of the computer output off-print ("hard copy") except that it carries a written description of what a number in its position would refer to. Table AIII-1 should be used as a guide when referring to Tables AIII-3 to AIII-85 inclusive (see Appendix IV, Section 3) which are actual computer print-outs of the statistical analysis performed on the results illustrated in Tables RC-1 to RC-7 and RE-1 to RE-21 (see Appendix IV, Section 1).

The probabilities that any change which occurred concomitantly with an infusion, whether control or experimental, could have been by chance alone was determined from the probability table (see Table AIII-2 in Appendix IV, Section 3) using the T-value and degrees of freedom obtained from the use of the statistical program "DO" (see Fig. AII-1, A).

Results Tables RC-9 (controls) and RE-23 (experimentals) depict the direction of change of all measured parameters and whether or not those changes were significant either to the $P < 0.05$ or $P < 0.01$ levels. This factor (significance of change) was obtained through use of the statistical programs described here.

FORMAT OF OUTPUT FROM STATISTICAL PROGRAMS

sign of t value (i.e. - t indicates that the
infusion value was up from pre-infusion levels)
indicates direction of responses

t-value	PERIPHERAL CORONARY PRESSURE			
mean pre-infus.	degrees of freedom	-----	-----	
mean infus.	variance of pre-infus.	stan. dev. pre-infus.	stan. error mean pre-infus.	
	variance infus.	stan. dev. infus.	stan. error mean infus.	
	AORTIC BLOOD PRESSURE			

same as above

LEFT DESCENDING BLOOD FLOW

same as above

TOTAL RESISTANCE

same as above

VESSEL ELEMENT RESISTANCE

same as above

PERIPHERAL CORONARY RESISTANCE

same as above

CORRELATION COEFFICIENT *2

same as above

APPENDIX IV

1. EXPERIMENTAL RESULTS RELATING
 TO PERFUSION EXPERIMENTS

A. Control Saline Infusion Results

Tables RC-1 to RC-7 are the results of control experiments referred to in the results section of this thesis.

B. Experimental Adrenaline Infusion Results

Tables RE-1 to RE-21 are the results of experimental exercises referred to in the results section of this thesis.

TABLES RC-1 TO RC-7

The table number (i.e. RC-1) also refers to the dog or experiment number in Table R-1A (i.e. RC-1) from which the particulars (i.e. 9 kg, 1 yr. old, ♀, 3 infusions following a coronary occlusion of duration 7 minutes) of the control animal, RC-1, may be obtained. In these tables, values are in the following units:

P.C.P. (peripheral coronary pressure) - mm Hg;

A.B.P. (aortic blood pressure) - mm Hg;

FLOW (flow) - ml/min;

C.R. (total left descending coronary vascular resistance)
- Newton x second x cm^{-5} ;

C.V.R. (left descending coronary vessel element resistance)
- Newton x second x cm^{-5} ;

P.C.R. (left descending peripheral coronary vascular resistance) - Newton x second x cm^{-5} ;

C.C.² (correlation coefficient squared) - (see Appendix I for explanation of correlation coefficient).

TABLE RC-1

EXPERIMENT NO. RC-1

SALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
22.00	70.00	5.610	9.957	6.828	3.129	0.988
20.00	51.00	6.460	6.300	3.829	2.471	0.987
21.00	72.00	6.110	9.404	6.661	2.743	0.999
19.00	65.00	3.820	13.579	9.609	3.969	0.953
16.00	66.00	3.890	13.539	10.257	3.282	0.946
16.00	61.00	5.380	9.048	6.675	2.373	0.965

(b) Infusion Data

17.00	53.00	3.360	12.587	8.550	4.037	0.953
19.00	50.00	3.740	10.668	6.614	4.054	0.962
22.00	53.00	4.910	8.614	5.038	3.576	0.991
21.00	48.00	6.310	6.070	3.415	2.656	0.965
21.00	58.00	4.070	11.372	7.255	4.117	0.986
14.00	53.00	5.570	7.593	5.587	2.006	0.961

SALINE INFUSION NO. 2

(a) Pre-Infusion Data

14.00	52.00	2.690	15.426	11.273	4.153	0.982
20.00	31.00	6.260	3.952	1.402	2.550	0.817
18.00	35.00	5.590	4.996	2.427	2.570	0.979
17.00	30.00	4.230	5.660	2.452	3.207	0.903
16.00	37.00	3.450	8.558	4.857	3.701	0.937
11.00	34.00	3.370	8.051	5.446	2.605	0.940

TABLE RC-1 (cont.)

(b) Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
15.00	29.00	2.920	7.925	3.826	4.099	0.975
14.00	41.00	10.940	2.991	1.969	1.021	0.768
13.00	28.00	5.270	4.240	2.271	1.969	0.980
15.00	24.00	1.830	10.466	3.925	6.541	0.989
11.00	23.00	9.670	1.898	0.990	0.908	0.995
7.00	15.00	5.880	2.036	1.086	0.950	0.936

SALINE INFUSION NO. 3

(a) Pre-Infusion Data

7.00	33.00	2.990	8.807	6.939	1.868	0.942
7.00	32.00	2.850	8.960	7.000	1.960	0.976
5.00	13.00	3.960	2.620	1.612	1.008	0.998
8.00	13.00	2.770	3.745	1.440	2.305	0.988
4.00	10.00	3.860	2.067	1.240	0.827	0.987
8.00	20.00	2.960	5.392	3.235	2.157	0.983

(b) Infusion Data

7.00	25.00	3.090	6.456	4.649	1.808	0.998
4.00	27.00	3.050	7.064	6.018	1.047	0.971
2.00	27.00	2.980	7.230	6.695	0.536	0.992
2.00	18.00	1.170	12.277	10.913	1.364	0.999
0.00	13.00	1.650	6.287	6.287	0.000	0.982
6.00	15.00	5.570	2.149	1.289	0.860	0.864

TABLE RC-2

EXPERIMENT NO. RC-2

SALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
40.00	117.00	12.340	7.566	4.979	2.587	0.974
40.00	104.00	6.040	13.470	8.456	5.285	1.000
45.00	100.00	8.430	9.466	5.206	4.260	0.928
40.00	97.00	5.960	12.988	7.632	5.356	0.999
32.00	96.00	7.790	9.834	6.556	3.278	0.994

(b) Infusion Data

32.00	93.00	6.500	11.418	7.489	3.929	0.948
31.00	83.00	4.800	13.799	8.645	5.154	0.984
30.00	78.00	5.200	11.970	7.366	4.604	0.985
31.00	85.00	5.320	12.750	8.100	4.650	0.989
31.00	103.00	10.690	7.689	5.375	2.314	0.946

SALINE INFUSION NO. 2

(a) Pre-Infusion Data

28.00	87.00	7.790	8.912	6.044	2.868	0.992
27.50	68.00	3.070	17.676	10.527	7.148	0.993
28.00	89.00	5.850	12.141	8.321	3.819	0.986
28.00	76.00	4.330	14.006	8.846	5.160	0.889
26.00	65.00	3.210	16.159	9.695	6.464	0.996

TABLE RC-2 (cont.)

(b) Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
25.00	58.00	2.410	19.205	10.927	8.278	0.935
25.00	71.00	6.560	8.637	5.596	3.041	0.962
25.00	56.00	2.330	19.179	10.616	8.562	0.888
25.00	68.00	2.400	22.610	14.297	8.313	0.971
25.00	55.00	2.780	15.788	8.612	7.176	0.995

SALINE INFUSION NO. 3

(a) Pre-Infusion Data

25.00	67.00	5.000	10.693	6.703	3.990	0.996
25.00	55.00	2.370	18.519	10.101	8.418	0.964
24.00	65.00	2.180	23.794	15.008	8.785	0.968
24.00	55.00	2.360	18.597	10.482	8.115	0.963

(b) Infusion Data

22.00	47.00	4.260	8.804	4.683	4.121	0.969
20.00	41.00	2.450	13.354	6.840	6.514	0.942
21.00	43.00	3.330	10.305	5.272	5.032	0.996
22.50	38.00	0.960	31.588	12.884	18.703	0.900

SALINE INFUSION NO. 4

(a) Pre-Infusion Data

23.00	44.00	1.530	22.949	10.953	11.996	0.976
22.50	42.00	1.970	17.013	7.899	9.114	0.936
23.00	35.00	1.220	22.893	7.849	15.044	0.998

TABLE RC-2 (cont.)

(b) Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
22.00	35.00	1.200	23.275	8.645	14.630	0.998
22.00	35.00	1.200	23.275	8.645	14.630	0.998
21.00	34.00	1.200	22.610	8.645	13.965	0.998

TABLE RC-3

EXPERIMENT NO. RC-3

SALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
22.00	116.00	16.560	5.590	4.530	1.060	0.993
24.00	116.00	10.880	8.508	6.748	1.760	0.999
19.00	116.00	11.890	7.785	6.510	1.275	0.999
20.00	112.00	16.730	5.819	4.865	0.954	0.995

(b) Infusion Data

19.00	120.00	15.030	6.371	5.362	1.009	1.000
20.00	114.00	13.410	6.784	5.594	1.190	0.998
20.00	116.00	11.790	7.851	6.498	1.354	0.986
20.00	120.00	13.150	7.282	6.068	1.214	0.996

SALINE INFUSION NO. 2

(a) Pre-Infusion Data

18.00	112.00	12.820	6.972	5.851	1.120	0.993
24.00	116.00	12.330	7.508	5.954	1.553	0.999
18.00	112.00	11.620	7.692	6.455	1.236	0.979
24.00	116.00	12.130	7.631	6.052	1.579	0.987

(b) Infusion Data

24.00	116.00	10.360	8.935	7.086	1.849	0.997
24.00	116.00	9.700	9.543	7.569	1.974	0.998
18.00	112.00	9.140	9.779	8.207	1.572	1.000
20.00	120.00	13.900	6.889	5.741	1.148	0.996

TABLE RC-3 (cont.)

SALINE INFUSION NO. 3

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
22.00	116.00	11.580	7.994	6.478	1.516	0.986
22.00	112.00	10.210	8.754	7.034	1.719	0.985
24.00	116.00	10.850	8.532	6.766	1.765	0.999
24.00	116.00	7.930	11.673	9.258	2.415	0.992

(b) Infusion Data

26.00	112.00	8.320	10.742	8.249	2.494	0.996
28.00	112.00	8.730	10.238	7.678	2.559	1.000
24.00	112.00	7.170	12.465	9.794	2.671	1.000
20.00	98.00	7.560	10.344	8.233	2.111	0.993

SALINE INFUSION NO. 4

(a) Pre-Infusion Data

20.00	101.00	7.060	11.416	9.156	2.261	0.997
20.00	100.00	6.900	11.565	9.252	2.313	0.992
20.00	100.00	12.180	6.552	5.241	1.310	0.991
20.00	104.00	8.380	9.904	7.999	1.905	0.996

(b) Infusion Data

20.00	106.00	6.740	12.550	10.182	2.368	1.000
20.00	104.00	7.240	11.463	9.259	2.204	0.992
20.00	100.00	6.620	12.054	9.664	2.411	0.992
22.00	104.00	5.90	13.948	10.998	2.951	0.986

TABLE RC-3 (cont.)

SALINE INFUSION NO. 5

(a) Pre-Infusion Data

24.00	102.00	8.210	9.914	7.581	2.333	1.000
24.00	102.00	6.670	12.203	9.332	2.871	1.000
22.00	102.00	7.760	10.489	8.227	2.262	0.993
20.00	104.00	7.340	11.307	9.132	2.174	1.000

(b) Infusion Data

22.00	100.00	11.330	7.043	5.494	1.550	0.998
24.00	104.00	8.320	9.975	7.673	2.302	0.974
24.00	104.00	8.190	10.133	7.795	2.338	0.991
22.00	102.00	7.740	10.516	8.248	2.268	0.987

TABLE RC-4

EXPERIMENT NO. RC-4

SALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
25.90	128.00	10.220	9.995	7.972	2.022	0.977
23.50	125.00	7.290	13.682	11.111	2.572	0.982
25.90	128.00	9.620	10.618	8.469	2.148	0.960
29.70	132.00	10.640	9.900	7.672	2.227	0.996

(b) Infusion Data

25.90	128.00	7.930	12.881	10.274	2.606	0.994
24.30	126.00	8.190	12.277	9.909	2.368	0.997
17.20	112.00	6.790	13.163	11.141	2.021	0.996
16.70	110.00	6.320	13.889	11.781	2.109	0.994

SALINE INFUSION NO. 2

(a) Pre-Infusion Data

16.10	106.00	6.430	13.155	11.157	1.998	0.996
16.30	96.00	10.560	7.255	6.023	1.232	0.991
16.30	96.00	8.750	8.755	7.269	1.487	0.993
16.60	94.00	8.630	8.692	7.157	1.535	0.998

(b) Infusion Data

16.40	95.00	10.050	7.543	6.241	1.302	0.988
15.90	102.00	12.110	6.721	5.674	1.048	0.994
16.60	94.00	9.870	7.600	6.258	1.342	1.000
16.30	96.00	9.510	8.056	6.688	1.368	0.994

TABLE RC-4 (cont.)
SALINE INFUSION NO. 3

(a) Pre-Infusion Data

16.00	104.00	12.070	6.876	5.818	1.058	0.985
16.00	100.00	12.150	6.568	5.517	1.051	0.969
16.30	96.00	10.520	7.282	6.046	1.236	0.997
16.10	97.00	10.950	7.069	5.888	1.181	0.995

(b) Infusion Data

16.00	104.00	12.370	6.709	5.677	1.032	1.000
16.10	98.00	11.650	6.713	5.610	1.103	0.999
16.00	100.00	12.650	6.308	5.299	1.009	0.992
16.30	96.00	11.900	6.438	5.345	1.093	0.994

TABLE RC-5
 EXPERIMENT NO. RC-5
 SALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
40.00	140.00	13.480	8.288	5.920	2.368	0.999
37.00	132.00	12.180	8.648	6.224	2.424	0.997
43.00	142.00	12.900	8.784	6.124	2.660	0.990
37.00	134.00	13.110	8.157	5.904	2.252	0.983
40.00	136.00	11.810	9.190	6.487	2.703	0.995
45.00	150.00	16.370	7.312	5.119	2.194	0.985
40.00	140.00	15.460	7.226	5.162	2.065	0.988

(b) Infusion Data

42.00	144.00	12.710	9.041	6.404	2.637	0.993
45.00	150.00	16.360	7.317	5.122	2.195	0.992
40.00	136.00	11.460	9.470	6.685	2.785	0.991
45.00	148.00	13.690	8.627	6.004	2.623	0.998
40.00	134.00	12.560	8.514	5.972	2.541	0.994
40.00	134.00	12.780	8.367	5.869	2.498	0.998
44.00	146.00	15.340	7.595	5.306	2.289	0.997

TABLE RC-6
 EXPERIMENT NO. RC-6
 SALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
17.00	55.00	7.780	5.641	3.898	1.744	0.998
17.00	57.00	9.150	4.971	3.489	1.483	0.987
17.00	55.00	7.820	5.613	3.878	1.735	1.000
16.00	53.00	7.570	5.587	3.900	1.687	0.998
16.00	54.00	7.630	5.648	3.974	1.673	0.998

(b) Infusion Data

16.00	54.00	7.780	5.539	3.898	1.641	0.998
16.00	54.00	8.500	5.070	3.568	1.502	1.000
17.00	56.00	9.840	4.541	3.163	1.379	0.992
17.00	56.00	9.480	4.714	3.283	1.431	0.996
17.00	57.00	10.450	4.353	3.055	1.298	0.987

SALINE INFUSION NO. 2

(a) Pre-Infusion Data

17.00	56.00	9.390	4.739	3.314	1.445	0.996
17.00	56.00	10.270	4.351	3.030	1.321	0.993
17.00	55.00	10.360	4.236	2.927	1.309	0.988
17.00	56.00	9.970	4.482	3.122	1.361	1.000
16.00	54.00	8.330	5.173	3.640	1.533	0.998

TABLE RC-6 (cont.)

(b) Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
17.00	56.00	10.910	4.096	2.853	1.243	0.999
17.00	57.00	11.070	4.109	2.883	1.225	0.996
16.00	54.00	10.430	4.132	2.907	1.224	0.998
17.00	55.00	9.320	4.709	3.254	1.456	1.000
17.00	56.00	10.700	4.176	2.909	1.268	0.998

SALINE INFUSION NO. 3

(a) Pre-Infusion Data

21.00	74.00	6.610	8.934	6.398	2.535	0.962
21.00	84.00	10.050	6.670	5.002	1.667	0.999
21.00	88.00	11.150	6.298	4.795	1.503	0.992
21.00	90.00	10.080	7.125	5.462	1.662	0.997

(b) Infusion Data

21.00	88.00	10.930	6.425	4.892	1.533	0.998
20.00	70.00	7.780	7.180	5.129	2.051	0.996
21.00	88.00	9.880	7.108	5.412	1.696	0.999
21.00	80.00	10.270	6.216	4.584	1.632	0.999
21.00	78.00	12.850	4.844	3.540	1.304	0.996

SALINE INFUSION NO. 4

(a) Pre-Infusion Data

21.00	74.00	13.310	4.437	3.178	1.259	0.997
19.00	64.00	8.700	5.870	4.128	1.743	0.999

TABLE RC-6 (cont.)

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
20.00	68.00	10.030	5.410	3.819	1.591	0.994
20.00	66.00	8.780	5.999	4.181	1.818	0.998
20.00	67.00	9.650	5.541	3.887	1.654	1.000

(b) Infusion Data

19.00	63.00	9.360	5.371	3.751	1.620	0.998
19.00	63.00	8.710	5.772	4.031	1.741	1.000
19.00	63.00	9.360	5.371	3.751	1.620	0.992
20.00	66.00	9.260	5.688	3.964	1.724	0.997
19.00	62.00	8.340	5.932	4.114	1.818	0.994

SALINE INFUSION NO. 5

(a) Pre-Infusion Data

19.00	64.00	8.700	5.870	4.128	1.743	0.999
19.00	65.00	9.040	5.738	4.061	1.677	0.998
19.00	64.00	9.540	5.353	3.764	1.589	1.000
18.00	60.00	8.400	5.700	3.990	1.710	0.999
19.00	62.00	8.780	5.635	3.908	1.727	0.998

(b) Infusion Data

18.00	60.00	7.630	6.275	4.393	1.883	0.999
18.00	60.00	9.050	5.291	3.703	1.587	0.998
17.00	56.00	7.950	5.621	3.915	1.706	0.992
18.00	60.00	8.880	5.392	3.774	1.618	0.998
17.00	56.00	8.070	5.538	3.857	1.681	0.998

TABLE RC-7

EXPERIMENT NO. RE-7

SALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
20.00	128.00	11.720	8.715	7.354	1.362	0.970
20.00	77.00	8.020	7.662	5.672	1.990	0.999
20.00	89.00	9.700	7.322	5.676	1.645	1.000

(b) Infusion Data

30.00	94.00	11.000	6.819	4.643	2.176	0.967
35.00	88.00	12.230	5.742	2.458	2.284	0.980
38.00	84.00	7.590	8.832	4.836	3.995	0.988
46.00	94.00	8.630	8.692	4.438	4.254	0.990

SALINE INFUSION NO. 2

(a) Pre-Infusion Data

12.00	96.00	7.580	10.107	8.843	1.263	0.987
17.00	105.00	5.670	14.778	12.385	2.393	0.994
20.00	113.00	8.180	11.024	9.073	1.951	0.998
12.00	62.00	4.160	11.893	9.591	2.302	0.983

(b) Infusion Data

11.00	61.00	1.960	24.836	20.357	4.479	0.229
14.00	80.00	6.010	10.622	8.763	1.859	0.999
16.00	90.00	11.710	6.133	5.043	1.090	0.962
16.00	80.00	5.010	12.743	10.513	2.230	0.999
15.00	77.00	4.980	12.339	9.935	2.404	0.999

TABLE RC-7 (cont.)

SALINE INFUSION NO. 3

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
16.00	78.00	4.560	13.650	10.850	2.800	0.991
10.00	80.00	4.820	13.245	11.589	1.656	0.962
15.00	75.00	4.180	14.318	11.455	2.864	0.985
14.00	75.00	4.040	14.814	12.049	2.765	0.998
15.00	74.00	4.810	12.277	9.788	2.489	0.994

(b) Infusion Data

10.00	57.00	4.240	10.728	8.846	1.882	0.998
12.00	59.00	3.680	12.794	10.192	2.602	0.988
12.00	58.00	3.310	13.983	11.090	2.893	0.995
12.00	58.00	3.190	14.509	11.507	3.002	0.976

TABLES RE-1 TO RE-21

The table number (i.e. RE-1) also refers to the dog or experiment number in Table R-1B (i.e. RE-1) from which the particulars (i.e. 6.5 kg, 14 yr. old, 0⁷, 3 infusions following a coronary occlusion of duration 4 minutes) of the experimental animal, RE-1 may be obtained. In these tables, values are in the following units:

P.C.P. (peripheral coronary pressure) - mm Hg;

A.B.P. (aortic blood pressure) - mm Hg;

FLOW (flow) - ml/min;

C.R. (total left descending coronary vascular resistance)
- Newton x second x cm⁻⁵;

C.V.R. (left descending coronary vessel element resistance)
- Newton x second x cm⁻⁵;

P.C.R. (left descending peripheral coronary vascular resistance) - Newton x second x cm⁻⁵;

C.C.² (correlation coefficient squared) - (see Appendix I for explanation of correlation coefficient).

TABLE RE-1
EXPERIMENT NO. RE-1
ADRENALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
11.00	77.00	25.870	2.375	2.036	0.339	0.994
10.00	43.00	6.930	4.952	3.800	1.152	0.962
12.00	68.00	15.230	3.563	2.934	0.629	0.999

(b) Infusion Data

14.00	113.00	19.060	4.731	4.145	0.586	0.938
13.00	105.00	13.100	6.396	5.604	0.792	0.944
12.00	95.00	9.410	8.056	7.039	1.018	0.989
12.00	85.00	6.840	9.917	8.517	1.400	0.976
11.00	78.00	6.160	10.105	8.680	1.425	0.966
11.00	70.00	6.490	8.607	7.255	1.353	0.998
11.00	74.00	8.770	6.733	5.732	1.001	0.991
11.00	77.00	5.260	11.682	10.013	1.669	0.999

ADRENALINE INFUSION NO. 2

(a) Pre-Infusion Data

9.00	36.00	2.390	12.020	9.015	3.005	0.891
8.00	28.00	6.250	3.575	2.554	1.021	0.995
7.00	44.00	8.580	4.092	3.441	0.651	0.979

TABLE RE-1 (cont.)

(b) Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
9.00	54.00	9.300	4.634	3.861	0.772	0.985
9.00	52.00	5.580	7.437	6.149	1.287	0.871
9.00	53.00	7.280	5.810	4.823	0.987	0.968
6.00	28.00	6.840	3.267	2.567	0.700	0.994

ADRENALINE INFUSION NO. 3

(a) Pre-Infusion Data

7.50	21.00	1.800	9.310	5.985	3.325	0.983
6.00	24.00	3.670	5.219	3.914	1.305	0.983

(b) Infusion Data

6.00	24.00	3.670	5.219	3.914	1.305	0.983
6.00	24.00	2.250	8.512	6.384	2.128	0.968
6.00	19.00	2.520	6.017	4.117	1.900	0.984

TABLE RE-2

EXPERIMENT NO. RE-2

ADRENALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
5.00	26.00	1.560	13.300	10.742	2.558	0.824
6.00	38.00	5.130	5.711	4.809	0.902	0.995
7.00	35.00	1.120	24.938	19.950	4.988	1.000
7.50	68.00	1.090	49.783	44.293	5.491	1.000

(b) Infusion Data

10.00	130.00	12.970	7.998	7.383	0.615	0.994
11.00	133.00	9.880	10.742	9.854	0.888	0.992
12.00	172.00	23.860	5.753	5.351	0.401	0.974
12.00	156.00	14.310	8.699	8.030	0.669	0.974

ADRENALINE INFUSION NO. 2

(a) Pre-Infusion Data

7.00	40.00	8.320	3.837	3.165	0.671	0.964
7.00	36.00	3.360	8.550	6.887	1.663	0.991
7.00	21.00	2.460	6.812	4.541	2.271	0.991
6.00	16.00	2.030	6.290	3.931	2.359	0.989

(b) Infusion Data

6.00	21.00	1.740	9.631	6.879	2.752	0.981
5.00	28.00	2.140	10.441	8.577	1.864	0.986
5.00	26.00	3.160	6.566	5.303	1.263	0.998

TABLE RE-3
 EXPERIMENT NO. RE-3
 ADRENALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
10.00	70.00	3.070	18.195	15.596	2.599	0.993
10.00	75.00	3.040	19.688	17.063	2.625	0.994

(b) Infusion Data

11.00	143.00	6.530	14.475	16.131	1.344	0.916
12.00	173.00	6.400	21.571	20.075	1.496	0.995
13.00	176.00	5.680	24.727	22.900	1.826	0.939
13.50	178.00	6.390	22.229	20.543	1.686	0.995
13.00	171.00	6.530	20.897	19.308	1.589	0.989
12.50	160.00	4.490	28.437	26.215	2.222	0.990

ADRENALINE INFUSION NO. 2

(a) Pre-Infusion Data

8.500	71.00	5.160	10.980	9.666	1.315	0.924
7.500	72.00	4.750	12.096	10.836	1.260	0.934
7.500	67.00	4.820	11.093	9.851	1.242	0.935
7.500	78.00	8.580	7.255	6.557	0.698	0.933
7.500	87.00	4.620	15.027	13.732	1.295	0.931
7.500	84.00	2.590	25.881	23.570	2.311	0.992
7.500	74.00	3.110	18.988	17.063	1.924	0.947
7.500	61.00	2.680	18.163	15.930	2.233	0.816

TABLE RE-3 (cont.)

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
7.50	56.00	6.850	6.524	5.650	0.874	0.996
8.50	45.00	4.390	8.180	6.635	1.545	0.977
10.00	80.00	6.180	10.330	9.039	1.291	0.980
11.50	137.00	5.520	19.805	18.143	1.662	0.924
12.50	163.00	7.560	17.206	15.886	1.319	0.988
12.50	163.00	7.690	16.915	15.618	1.297	0.940
12.50	164.00	6.690	19.562	18.071	1.491	0.973
12.50	155.00	5.100	24.253	22.297	1.956	0.938

ADRENALINE INFUSION NO. 3

(a) Pre-Infusion Data

7.50	26.00	2.620	7.919	5.635	2.284	0.903
7.50	53.00	5.560	7.607	6.530	1.076	0.926
7.50	55.00	4.900	8.957	7.736	1.221	0.894
7.50	57.00	3.990	11.400	9.900	1.500	0.858
7.50	55.00	5.510	7.966	6.879	1.086	0.865
7.50	59.00	3.870	12.166	10.619	1.547	0.857
7.50	45.00	4.230	8.489	7.074	1.415	0.865
7.50	44.00	1.880	18.677	15.493	3.184	0.925

(b) Infusion Data

8.00	54.00	3.110	13.856	11.803	2.053	0.904
8.50	61.00	2.940	16.557	14.250	2.307	0.819

TABLE RE-3 (cont.)

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
8.50	61.00	3.330	14.618	12.581	2.037	0.886
8.00	59.00	3.470	13.568	11.729	1.840	0.878
8.50	44.00	3.240	10.837	8.744	2.094	0.909
8.50	58.00	3.080	15.027	12.825	2.202	0.903
8.50	71.00	4.370	12.965	11.413	1.552	0.890
8.50	66.00	3.290	16.009	13.947	1.062	0.885
8.50	61.00	3.330	14.618	12.581	2.037	0.798
8.50	59.00	2.960	15.906	13.615	2.292	0.820
8.50	60.00	3.470	13.798	11.844	1.955	0.878

TABLE RE-4

EXPERIMENT NO. RE-4

ADRENALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
15.00	101.00	23.070	3.494	2.975	0.519	0.954
15.00	95.00	10.230	7.411	6.240	1.170	0.945
15.00	89.00	10.130	7.011	5.829	1.182	0.997
15.00	90.00	6.140	11.697	9.748	1.950	0.999
15.00	87.00	6.460	10.747	8.894	1.853	0.972

(b) Infusion Data

16.00	85.00	12.300	5.515	4.477	1.038	0.937
18.00	115.00	22.490	4.080	3.442	0.639	0.988
20.00	127.00	22.380	4.528	3.815	0.713	0.887
22.00	126.00	25.090	4.007	3.308	0.700	0.983
22.00	127.00	17.480	5.798	4.793	1.004	0.976
20.00	116.00	15.720	5.889	4.873	1.015	0.972

ADRENALINE INFUSION NO. 2

(a) Pre-Infusion Data

16.00	57.00	5.730	7.938	5.710	2.228	0.989
16.00	60.00	4.250	11.266	8.262	3.004	0.991
16.00	60.00	7.040	6.801	4.987	1.814	0.997

(b) Infusion Data

17.00	71.00	7.170	7.902	6.010	1.892	0.976
18.00	114.00	12.650	7.191	6.056	1.135	0.862

TABLE RE-4 (cont.)

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
19.00	140.00	16.220	6.888	5.953	0.935	0.969
20.00	142.00	16.040	7.065	6.070	0.995	0.983
20.00	145.00	17.550	6.593	5.684	0.909	0.984
20.00	154.00	21.260	5.780	5.030	0.751	0.997

ADRENALINE INFUSION NO. 3

(a) Pre-Infusion Data

16.00	42.00	4.930	6.798	4.209	2.590	0.984
15.00	37.00	3.060	9.649	5.737	3.912	0.991
14.00	42.00	6.360	5.270	3.513	1.757	0.962
13.00	40.00	6.510	4.903	3.310	1.594	0.964
12.00	37.00	4.340	6.803	4.597	2.206	0.983
11.00	39.00	4.780	6.511	4.674	1.836	0.982
11.00	35.00	3.490	8.003	5.488	2.515	0.998
11.00	61.00	8.000	6.085	4.988	1.097	0.986

(b) Infusion Data

11.00	69.00	6.440	8.550	7.187	1.363	0.892
12.00	81.00	9.760	6.623	5.642	0.981	0.990
13.00	116.00	14.280	6.482	5.756	0.726	0.842
15.00	119.00	9.670	9.820	8.582	1.238	0.988
15.00	126.00	17.690	5.684	5.007	0.677	0.999
16.00	139.00	18.680	5.938	5.254	0.684	0.976
14.00	117.00	17.040	5.479	4.824	0.656	0.967
14.00	119.00	16.660	5.700	5.029	0.671	0.976

TABLE RE-4 (cont.)

ADRENALINE INFUSION NO. 4

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
13.00	57.00	6.160	6.384	5.700	1.684	0.941
13.00	60.00	6.950	6.889	5.397	1.493	0.986
12.50	37.00	4.740	6.229	4.125	2.104	0.969
12.00	39.00	3.120	9.975	6.906	3.069	0.827
13.00	39.00	4.760	6.538	4.359	2.179	0.984
14.00	39.00	4.850	6.417	4.113	2.304	0.984
16.00	35.00	7.080	3.945	2.142	1.803	0.679
17.00	42.00	2.980	11.247	6.695	4.552	0.992

(b) Infusion Data

17.00	37.00	3.130	9.433	5.099	4.334	0.991
16.00	42.00	3.160	10.606	6.566	4.041	0.828
16.00	48.00	5.150	7.438	4.958	2.479	0.983
16.00	45.00	2.780	12.917	8.324	4.593	0.947
18.00	52.00	4.480	9.263	6.056	3.206	0.978
18.00	55.00	4.720	9.299	6.256	3.043	0.966

TABLE RE-5
EXPERIMENT NO. RE-5
ADRENALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
11.00	89.00	23.300	3.048	2 671	0.377	0.993
11.00	86.00	21.370	3.211	2.801	0.411	0.968
11.00	82.00	9.330	7.014	6.073	0.941	0.988
12.00	87.00	10.360	6.701	5.777	0.924	0.944
11.00	79.00	11.640	5.416	4.662	0.754	0.982
12.00	86.00	8.980	7.642	6.576	1.066	0.996
13.00	86.00	9.260	7.411	6.291	1.120	0.979
13.00	83.00	7.590	8.726	7.360	1.367	0.971

(b) Infusion Data

13.00	99.00	11.560	6.834	5.937	0.897	0.982
13.00	97.00	9.390	8.243	7.139	1.105	0.989
14.00	128.00	12.690	8.049	7.169	0.880	0.976
15.00	143.00	11.450	9.966	8.921	1.045	0.997
15.00	151.00	10.230	11.779	10.609	1.170	0.998
16.00	161.00	10.020	12.822	11.548	1.274	0.964
15.00	149.00	5.590	21.270	19.129	2.141	0.992

ADRENALINE INFUSION NO. 2

(a) Pre-Infusion Data

13.00	73.00	7.930	7.346	6.038	1.308	0.995
13.00	83.00	8.550	7.747	7.533	1.213	0.994

TABLE RE-5 (cont.)

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R	P.C.R.	C.C. ²
13.00	87.00	6.950	9.898	8.497	1.493	0.992
12.00	77.00	10.640	5.775	4.875	0.900	0.984
13.00	93.00	14.670	5.059	4.352	0.707	0.994
13.00	90.00	14.390	4.991	4.270	0.721	0.997
13.00	105.00	10.160	4.156	3.642	0.515	0.962
10.00	80.00	7.400	8.627	7.549	1.078	0.994

(b) Infusion Data

11.00	90.00	8.300	8.653	7.595	1.058	0.987
11.00	90.00	9.760	7.359	6.459	0.899	0.995
12.00	100.00	7.230	11.037	9.713	1.324	0.986
14.00	119.00	10.760	8.825	7.787	1.038	0.996
13.00	121.00	9.410	10.261	9.159	1.102	0.988
14.00	132.00	13.130	8.023	7.172	0.851	0.96
14.00	130.00	12.900	8.042	7.176	0.866	0.998

ADRENALINE INFUSION NO. 3

12.00	75.00	6.270	9.545	8.018	1.527	0.988
13.00	83.00	9.030	7.335	6.186	1.149	0.988
13.00	81.00	7.770	8.319	6.984	1.335	0.960
13.00	89.00	7.890	9.002	7.687	1.315	0.976
13.00	94.00	8.410	8.919	7.686	1.234	0.980
13.00	89.00	7.610	9.333	7.970	1.363	0.993

TABLE RE-5 (cont.)

(b) Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
22.00	98.00	4.580	17.075	13.242	3.833	0.931
25.00	93.00	3.360	22.088	16.150	5.938	0.949
30.00	99.00	2.370	33.334	23.233	10.101	0.970
35.00	103.00	2.250	36.531	24.117	12.413	1.000

TABLE RE-6

EXPERIMENT NO. RE-6

ADRENALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
8.00	76.00	14.050	4.317	3.862	0.454	0.995
9.00	99.00	7.680	10.287	9.352	0.935	0.980
8.00	90.00	9.400	7.640	6.961	0.679	0.993

(b) Infusion Data

8.00	90.00	7.630	9.413	8.576	0.837	0.990
10.00	122.00	15.220	6.397	5.872	0.524	0.999
8.00	62.00	5.580	8.867	7.723	1.144	0.994
9.00	91.00	45.540	1.595	1.437	0.158	0.992

TABLE RE-7

EXPERIMENT NO. RE-7

ADRENALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
16.00	85.00	6.740	10.064	8.169	1.894	0.993
22.00	77.00	4.600	13.358	9.541	3.817	0.980
16.00	80.00	10.420	6.127	4.901	1.225	0.967

(b) Infusion Data

21.00	92.00	7.260	10.112	7.804	2.308	0.994
15.00	103.00	5.680	14.471	12.363	2.107	0.954
12.00	111.00	9.190	9.639	8.597	1.042	0.987
12.00	106.00	10.700	7.905	7.010	0.895	0.938

ADRENALINE INFUSION NO. 2

(a) Pre-Infusion Data

15.00	92.00	6.070	12.095	10.123	1.972	0.999
8.00	75.00	3.800	15.750	14.070	1.680	0.927
13.00	71.00	4.040	14.024	11.456	2.568	0.985
8.00	72.00	3.950	14.546	12.930	1.616	0.969

(b) Infusion Data

11.00	74.00	5.430	10.875	9.259	1.617	0.993
15.00	81.00	5.650	11.440	9.322	2.119	0.855
15.00	83.00	6.630	9.990	8.185	1.805	0.979
8.00	77.00	3.910	15.715	14.082	1.633	0.968

TABLE RE-7 (cont.)

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
20.00	94.00	8.600	8.722	6.867	1.856	0.981
10.00	80.00	4.770	13.384	11.711	1.673	0.933

TABLE RE-8

EXPERIMENT NO. RE-8

ADRENALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
7.00	44.00	4.370	8.035	6.757	1.278	0.976
8.00	64.00	11.050	4.622	4.044	0.578	0.987
12.00	78.00	7.850	7.929	6.709	1.220	0.999
28.00	79.00	9.180	6.867	4.433	2.434	0.979
29.00	84.00	8.910	7.523	4.926	2.597	0.976

(b) Infusion Data

12.00	90.00	7.450	9.640	8.355	1.285	0.998
25.00	126.00	17.840	5.636	4.518	1.118	0.994
18.00	145.00	18.320	6.316	5.532	0.784	0.998
14.00	132.00	13.460	7.826	6.996	0.830	0.997
15.00	179.00	16.010	8.922	8.174	0.748	0.968
13.00	142.00	22.220	5.100	4.633	0.467	0.999

ADRENALINE INFUSION NO. 2

(a) Pre-Infusion Data

8.00	47.00	4.620	8.118	6.736	1.382	0.994
13.00	54.00	15.160	2.842	2.158	0.684	0.998
10.00	47.00	6.180	6.069	4.778	1.291	0.996
13.00	71.00	12.040	4.706	3.844	0.862	0.999
10.00	64.00	7.110	7.183	6.061	1.122	0.997
8.00	69.00	9.560	5.760	5.092	0.668	0.974

TABLE RE-8 (cont.)

(b) Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R	P.C.R.	C.C. ²
10.00	96.00	20.520	3.733	3.344	0.389	0.990
13.00	103.00	16.320	5.036	4.401	0.636	0.999
13.00	106.00	22.150	3.819	3.351	0.468	0.996
10.00	110.00	16.290	5.389	4.899	0.490	1.000
5.00	105.00	16.290	5.144	4.899	0.245	1.000

ADRENALINE INFUSION NO. 3

(a) Pre-Infusion Data

6.00	66.00	8.930	5.898	5.362	0.536	0.993
6.00	75.00	7.180	8.336	7.669	0.667	0.998
6.00	73.00	7.840	7.430	6.820	0.611	0.990
10.00	73.00	6.750	8.630	7.448	1.182	0.980
10.00	69.00	11.390	4.834	4.134	0.701	0.995
8.00	60.00	10.960	4.369	3.786	0.582	0.976
7.00	55.00	8.670	5.062	4.418	0.644	1.000
8.00	54.00	5.670	7.600	6.474	1.126	0.989
10.00	59.00	3.690	12.759	10.597	2.163	0.986

(b) Infusion Data

6.00	63.00	4.820	10.430	9.437	0.993	0.890
8.00	69.00	6.940	7.934	7.014	0.920	0.973
12.00	81.00	13.280	4.867	4.146	0.721	0.996
8.00	80.00	14.380	4.439	3.996	0.444	0.997

TABLE RE-8 (cont.)

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
12.00	92.00	14.900	4.927	4.285	0.643	0.999
10.00	87.00	14.690	4.726	4.183	0.543	1.000
8.00	81.00	8.630	7.490	6.750	0.740	0.981
13.00	60.00	11.160	4.290	3.361	0.930	0.999

TABLE RE-9

EXPERIMENT NO. RE-9

ADRENALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
35.00	106.00	8.680	9.745	6.527	3.218	0.993
30.00	82.00	7.920	8.262	5.239	3.023	0.874
30.00	98.00	10.370	7.541	5.233	2.390	0.983
35.00	68.00	7.260	7.474	3.627	3.847	0.989

(b) Infusion Data

50.00	103.00	9.320	8.819	4.538	4.281	0.992
77.00	196.00	23.870	6.552	3.978	2.547	0.995
75.00	181.00	14.570	9.913	5.806	4.108	0.925
51.00	102.00	6.860	11.865	5.933	5.933	0.984

ADRENALINE INFUSION NO. 2

(a) Pre-Infusion Data

25.00	37.00	1.680	17.575	5.700	11.875	0.984
25.00	63.00	6.550	7.675	4.630	3.046	0.990
31.00	79.00	10.060	6.267	3.808	2.459	0.990
25.00	64.00	8.520	5.994	3.653	2.342	0.997

(b) Infusion Data

38.00	84.00	8.110	8.265	4.526	3.739	0.992
28.00	73.00	5.100	11.422	7.041	4.381	0.897
41.00	90.00	9.330	7.698	4.191	3.507	0.999

TABLE RE-9 (cont.)

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
30.00	78.00	5.020	12.399	7.630	4.769	0.895
35.00	89.00	7.720	9.200	5.582	3.618	0.993
30.00	82.00	18.670	3.505	2.223	1.282	0.996
30.00	70.00	4.270	13.082	7.475	5.607	0.978
35.00	88.00	6.720	10.450	6.294	4.156	0.953
34.00	83.00	6.310	10.497	6.197	4.300	0.990

TABLE RE-10

EXPERIMENT NO. RE-10

ADRENALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
13.00	49.00	4.890	7.996	5.875	2.121	0.994
17.00	88.00	8.640	8.128	6.558	1.570	0.996
12.00	70.00	3.720	15.016	12.442	2.574	0.956
12.00	78.00	6.500	9.576	8.103	1.473	0.962
12.00	88.00	8.120	8.648	7.469	1.179	0.962
12.00	67.00	4.870	10.979	9.012	1.966	0.994

(b) Infusion Data

7.50	86.00	14.340	4.786	4.368	0.417	0.965
8.00	67.00	6.100	8.765	7.718	1.047	0.964
10.00	99.00	11.210	7.047	6.336	0.712	0.988
12.00	79.00	6.210	10.152	8.610	1.542	0.888
12.00	78.00	5.800	10.732	9.081	1.651	0.937
12.00	99.00	10.530	7.503	6.593	0.909	0.973
12.00	86.00	7.090	9.680	8.329	1.351	0.985
12.50	78.00	5.240	11.879	9.975	1.904	0.962
12.00	88.00	6.200	11.326	9.782	1.545	0.946
12.00	93.00	8.390	8.846	7.704	1.141	0.997
12.00	73.00	4.340	13.423	11.216	2.206	0.907
10.00	73.00	5.280	11.033	9.522	1.511	0.963
8.00	84.00	6.490	10.329	9.345	0.984	0.993
7.00	69.00	3.450	15.960	14.341	1.619	0.950

TABLE RE-11

EXPERIMENT NO. RE-11

ADRENALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
28.00	82.00	3.860	16.952	11.164	5.789	0.989
23.00	88.00	9.500	7.392	5.460	1.932	1.000
23.00	87.00	6.710	10.347	7.611	2.735	0.993
24.00	89.00	6.640	10.696	7.812	2.884	0.960
24.00	82.00	8.080	8.099	5.728	2.370	0.997
25.00	87.00	5.870	11.827	8.429	3.399	0.992
26.00	97.00	11.700	6.616	4.843	1.773	0.996
27.00	93.00	11.470	6.470	4.592	1.878	0.994
28.00	99.00	12.960	6.096	4.372	1.724	0.999
28.00	99.00	11.550	6.840	4.905	1.935	0.997

(b) Infusion Data

28.00	102.00	11.150	7.300	5.296	2.004	0.991
28.00	115.00	11.170	7.541	5.705	1.836	0.995
29.00	122.00	11.140	8.739	6.662	2.077	0.996
27.00	125.00	15.520	6.427	5.039	1.388	0.986
26.00	117.00	11.520	8.105	6.304	1.801	0.989
25.00	116.00	11.810	7.838	6.149	1.689	0.998

ADRENALINE INFUSION NO. 2

(a) Pre-Infusion Data

TABLE RE-11 (cont.)

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
45.00	99.00	3.200	24.688	13.466	11.222	0.953
42.00	77.00	4.240	14.492	6.587	7.905	0.995
36.00	66.00	4.240	12.422	5.646	6.775	0.982

(b) Infusion Data

25.00	100.00	8.540	9.344	7.008	2.336	0.999
27.00	106.00	8.460	9.999	7.452	2.547	0.980
28.00	107.00	6.570	12.996	9.595	3.401	0.992
29.00	125.00	5.850	17.051	13.095	3.956	0.985
29.00	122.00	4.660	20.892	15.926	4.966	0.960
32.00	118.00	4.250	22.156	16.148	6.008	0.998
48.00	114.00	3.540	25.698	14.878	10.820	0.987

TABLE RE-12

EXPERIMENT NO. RE-12

ADRENALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
26.00	93.00	11.340	6.544	4.715	1.830	0.987
25.00	81.00	7.130	9.066	6.268	2.798	0.979
28.00	111.00	7.490	11.826	8.843	2.983	0.987
27.00	107.00	7.280	11.729	8.769	2.960	0.989
25.00	104.00	6.590	12.594	9.566	3.027	0.996
23.00	102.00	6.590	12.351	9.566	2.785	0.996

(b) Infusion Data

28.00	112.00	16.530	5.407	4.055	1.352	0.975
28.00	123.00	16.260	6.037	4.662	1.372	0.992
28.00	112.00	10.610	8.424	6.318	2.106	0.996
28.00	138.00	16.710	6.590	5.253	1.337	0.983
28.00	122.00	12.080	8.059	6.210	1.850	0.964
28.00	131.00	20.090	5.203	4.091	1.112	0.992
28.00	124.00	13.770	7.186	5.563	1.623	0.999

TABLE RE-13

EXPERIMENT NO. RE-13

ADRENALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
14.00	74.00	8.070	7.317	5.933	1.384	0.953
14.00	69.00	7.160	7.690	6.130	1.560	0.979
14.00	73.00	8.980	6.487	5.243	1.244	0.994
15.00	82.00	12.050	5.430	4.437	0.993	0.993
15.00	79.00	9.530	6.615	5.359	1.256	0.992

(b) Infusion Data

16.00	81.00	10.210	6.331	5.080	1.251	0.984
16.00	87.00	12.710	5.462	4.458	1.005	0.982
15.00	87.00	11.190	6.204	5.135	1.070	0.998
15.00	82.00	9.490	6.895	5.634	1.261	0.984
15.00	82.00	9.880	6.623	5.412	1.212	0.999
15.00	82.00	9.000	7.271	5.941	1.330	0.976
14.00	75.00	7.870	7.605	6.185	1.420	0.997

TABLE RE-14

EXPERIMENT NO. RE-14

ADRENALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
12.00	76.00	7.740	7.836	6.598	1.237	0.954
14.00	78.00	9.900	6.287	5.159	1.128	0.996
14.00	88.00	12.740	5.512	4.635	0.877	0.994
14.00	88.00	11.710	5.997	5.043	0.954	0.993
13.00	86.00	8.500	8.074	6.853	1.220	0.942
12.00	76.00	7.970	7.610	6.408	1.202	0.878
12.00	76.00	8.080	7.506	6.321	1.185	1.000

(b) Infusion Data

44.00	100.00	10.650	7.493	4.196	3.297	0.975
28.00	186.00	32.090	4.625	3.929	0.696	0.987
28.00	212.00	35.270	4.797	4.163	0.634	0.974
20.00	200.00	41.360	3.859	3.473	0.386	0.976
20.00	196.00	40.380	3.873	3.478	0.395	0.991
20.00	188.00	39.330	3.814	3.409	0.406	0.975
20.00	182.00	39.650	3.663	3.260	0.403	0.982
16.00	120.00	20.870	4.588	3.977	0.612	0.968

ADRENALINE INFUSION NO. 2

(a) Pre-Infusion Data

13.00	60.00	5.940	8.061	6.314	1.746	0.999
12.00	52.00	4.650	8.924	6.865	2.059	0.981

TABLE RE-14 (cont.)

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
8.00	56.00	3.920	11.400	9.771	1.629	0.977
8.00	58.00	4.230	10.942	9.433	1.509	0.996
8.00	62.00	4.160	11.893	10.359	1.535	0.977

(b) Infusion Data

12.00	82.00	10.490	6.238	5.325	0.913	0.996
24.00	160.00	29.510	4.327	3.678	0.649	0.976
25.00	200.00	30.330	5.262	4.604	0.658	0.998
25.00	204.00	42.040	3.872	3.398	0.475	0.983
26.00	178.00	29.790	4.768	4.072	0.696	0.995
26.00	166.00	30.530	4.339	3.659	0.680	0.994

ADRENALINE INFUSION NO. 3

(a) Pre-Infusion Data

24.00	48.00	3.250	11.786	5.893	5.893	0.989
23.00	50.00	2.810	14.199	7.668	6.532	0.936
23.00	52.00	3.880	10.695	5.964	4.730	0.997

(b) Infusion Data

12.00	86.00	8.560	8.017	6.899	1.119	0.997
20.00	166.00	29.510	4.489	3.948	0.541	0.989
40.00	198.00	37.790	4.181	3.336	0.845	0.988
24.00	180.00	21.070	6.817	5.908	0.909	0.979
24.00	148.00	22.020	5.363	4.494	0.870	0.980
20.00	142.00	20.660	5.485	4.712	0.773	0.980
20.00	136.00	19.990	5.429	4.631	0.798	0.985

TABLE RE-15
 EXPERIMENT NO. RE-15
 ADRENALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
17.00	105.00	7.710	10.868	9.108	1.760	0.999
16.00	105.00	5.320	15.750	13.350	2.400	0.999
20.00	106.00	12.610	6.708	5.442	1.266	0.987
20.00	108.00	8.620	9.998	8.147	1.852	0.979
20.00	109.00	7.110	12.234	9.989	2.245	0.966
19.00	108.00	6.550	13.158	10.843	2.315	0.978

(b) Infusion Data

18.00	112.00	6.400	13.965	11.721	2.244	0.996
24.00	150.00	12.140	9.860	8.282	1.578	0.995
16.00	153.00	18.330	6.661	5.964	0.697	0.999
20.00	142.00	18.380	6.165	5.297	0.868	0.992
20.00	140.00	17.130	6.522	5.590	0.932	0.998
20.00	138.00	15.980	6.891	5.893	0.999	0.999

TABLE RE-16
 EXPERIMENT NO. RE-16
 ADRENALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
20.00	50.00	1.840	21.685	13.011	8.674	0.984
22.00	52.00	2.060	20.144	11.621	8.522	0.999
20.00	56.00	1.250	35.750	22.982	12.768	1.000
23.00	50.00	1.380	28.913	15.613	13.300	0.973
24.00	58.00	1.270	36.444	21.364	15.080	1.000
22.00	54.00	1.190	36.212	21.459	14.753	1.000

(b) Infusion Data

24.00	56.00	1.580	28.284	16.162	12.122	0.973
28.00	78.00	2.860	21.764	13.951	7.813	0.971
42.00	92.00	2.590	28.346	15.405	12.941	1.000
48.00	95.00	2.320	32.677	16.166	16.510	1.000
46.00	106.00	2.770	30.537	17.285	13.252	0.959

ADRENALINE INFUSION NO. 2

(a) Pre-Infusion Data

32.00	76.00	2.670	22.715	13.151	9.564	0.999
28.00	64.00	1.050	48.640	27.360	21.280	1.000
28.00	80.00	1.590	40.151	26.098	14.053	0.970
30.00	64.00	1.050	48.640	25.840	22.800	1.000
18.00	72.00	1.410	40.749	30.562	10.187	1.000

TABLE RE-16 (cont.)

P.C.P.	A.M.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
23.00	66.00	1.280	41.147	26.808	14.339	1.000
13.00	40.00	1.220	26.164	17.661	8.503	1.000
15.00	40.00	1.130	28.248	17.655	10.593	1.000
16.00	40.00	1.080	29.556	17.733	11.822	1.000

(b) Infusion Data

20.00	68.00	2.200	24.665	17.411	7.255	0.983
36.00	70.00	1.110	50.324	24.443	25.881	1.000
40.00	84.00	1.210	55.398	29.018	26.380	1.000
34.00	84.00	1.030	65.080	38.738	26.342	1.000
36.00	92.00	1.250	58.733	35.750	22.982	1.000

ADRENALINE INFUSION NO. 3

(a) Pre-Infusion Data

16.00	60.00	1.240	38.613	28.316	10.297	1.000
28.00	56.00	1.120	39.900	19.950	19.950	1.000
25.00	69.00	1.210	45.506	29.018	16.488	1.000
32.00	64.00	1.230	41.522	20.761	20.761	1.000
22.00	46.00	1.040	35.296	18.465	16.881	1.000
21.00	50.00	1.260	31.667	18.367	13.300	1.000
19.00	45.00	1.130	31.779	18.361	13.418	1.000
20.00	48.00	1.170	32.738	19.097	13.641	1.000
19.00	48.00	1.500	25.536	15.428	10.109	1.000
18.00	41.00	0.770	42.491	23.836	18.655	0.889

TABLE RE-16 (cont.)

(b) Infusion Data

P.C.P.	A.M.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
28.00	60.00	1.470	32.571	17.371	15.200	0.972
36.00	75.00	1.400	42.750	22.230	20.520	1.000
35.00	86.00	1.370	50.093	29.707	20.387	1.000
48.00	89.00	2.030	34.986	16.117	18.869	0.983
46.00	84.00	1.140	58.800	26.600	32.200	1.000

ADRENALINE INFUSION NO. 4

(a) Pre-Infusion Data

24.00	52.00	1.080	38.422	20.689	17.733	1.000
27.00	60.00	1.820	26.308	14.469	11.838	0.980
27.00	50.00	0.400	99.750	45.885	53.865	0.800
23.00	56.00	1.320	33.855	19.950	13.905	1.000

(b) Infusion Data

44.00	148.00	8.940	13.211	9.283	3.928	0.972
52.00	154.00	7.330	16.766	11.105	5.661	0.995
62.00	130.00	2.230	46.520	24.334	22.187	0.971
48.00	78.00	1.200	51.870	19.950	31.920	1.000

TABLE RE-17

EXPERIMENT NO. RE-17

ADRENALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R	P.C.R.	C.C. ²
28.00	130.00	11.080	9.363	7.346	2.017	0.988
30.00	124.00	8.990	11.007	8.344	2.663	0.999
32.00	124.00	9.160	10.803	8.015	2.788	1.000
44.00	112.00	4.340	20.594	12.503	8.090	0.998
44.00	110.00	3.870	22.682	13.609	9.073	0.985
44.00	112.00	3.770	23.707	14.394	9.314	0.999
48.00	112.00	4.590	19.474	11.127	8.345	0.989
46.00	112.00	4.940	18.092	10.662	7.431	0.963
44.00	116.00	6.430	14.396	8.936	5.461	0.995
48.00	118.00	3.670	20.164	11.961	8.202	0.989
46.00	114.00	3.770	24.131	14.394	9.737	0.999
44.00	116.00	4.720	19.612	12.173	7.439	0.988

(b) Infusion Data

48.00	116.00	4.990	18.551	10.875	7.676	0.999
40.00	122.00	5.920	16.445	11.053	5.392	0.984
48.00	148.00	7.900	14.950	10.101	4.849	0.986
44.00	152.00	7.500	16.173	11.491	4.682	0.953
44.00	148.00	7.690	15.358	10.792	4.566	0.991
44.00	144.00	8.320	13.812	9.591	4.220	0.985

TABLE RE-17 (cont.)

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
28.00	142.00	14.940	7.585	6.089	1.496	0.981
32.00	146.00	12.440	9.366	7.313	2.053	0.968
32.00	143.00	10.640	10.725	8.325	2.400	1.000
36.00	145.00	9.920	11.664	8.768	2.896	0.999
38.00	148.00	10.360	11.400	8.473	2.927	0.979
40.00	138.00	8.630	12.761	9.062	3.699	0.988
40.00	133.00	8.820	12.033	8.414	3.619	0.988
40.00	130.00	6.440	16.109	11.152	4.957	0.996
40.00	130.00	7.710	13.455	9.315	4.140	0.999
40.00	136.00	7.000	15.504	10.944	4.560	0.976

(b) Infusion Data

48.00	154.00	7.910	15.536	10.694	4.842	0.999
48.00	164.00	9.020	14.509	10.263	4.247	0.997
48.00	164.00	8.730	14.991	10.603	4.388	1.000
48.00	164.00	8.970	14.590	10.320	4.270	1.000

ADRENALINE INFUSION NO. 3

(a) Pre-Infusion Data

36.00	118.00	7.470	12.606	8.760	3.846	1.000
40.00	120.00	6.800	14.082	9.388	4.694	0.987
40.00	114.00	6.410	14.192	9.212	4.980	0.962
46.00	114.00	5.800	15.685	9.356	6.329	0.994
52.00	124.00	4.270	23.174	13.456	9.718	0.984

TABLE RE-17 (cont.)

(b) Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
56.00	132.00	6.180	17.045	9.814	7.231	0.997
80.00	148.00	6.760	17.471	8.027	9.444	0.996
56.00	156.00	10.350	12.028	7.710	4.318	0.998
48.00	152.00	10.430	11.630	7.957	3.672	0.991
48.00	154.00	10.170	12.084	8.317	3.766	0.999

TABLE RE-18
 EXPERIMENT NO. RE-18
 ADRENALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
22.00	100.00	7.560	10.556	8.233	2.322	0.993
24.00	104.00	7.420	11.185	8.604	2.581	1.000
24.00	102.00	7.020	11.595	8.867	2.728	0.985
24.00	100.00	11.540	6.915	5.255	1.660	0.999
24.00	98.00	8.160	9.584	7.237	2.347	0.999
24.00	100.00	7.370	10.828	8.229	2.599	0.993
24.00	102.00	7.030	11.578	8.854	2.724	0.993
24.00	102.00	6.780	12.005	9.181	2.825	1.000

(b) Infusion Data

27.00	124.00	10.910	9.070	7.095	1.975	0.988
27.00	128.00	10.560	9.673	7.632	2.040	0.990
27.00	132.00	11.510	9.152	7.280	1.872	0.996
27.00	134.00	12.600	8.487	6.777	1.710	0.994
25.00	100.00	9.830	8.118	6.089	2.030	0.988

TABLE RE-19

EXPERIMENT NO. RE-19

ADRENALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
25.00	68.00	1.920	28.262	17.872	10.391	0.983
32.00	86.00	1.430	47.992	30.134	17.857	0.970
28.00	148.00	6.920	17.067	13.838	3.229	0.974
30.00	148.00	12.640	9.344	7.450	1.894	0.980
31.00	84.00	2.080	32.227	20.334	11.893	1.000
34.00	90.00	1.490	48.201	29.992	18.209	0.970
34.00	89.00	1.930	36.799	22.741	14.058	0.982
33.00	88.00	4.340	16.181	10.113	6.068	0.985
35.00	92.00	4.760	15.424	9.556	5.868	0.999
37.00	95.00	4.160	18.224	11.126	7.098	0.999
40.00	100.00	4.260	18.732	11.239	7.493	0.985
39.00	98.00	4.930	15.863	9.550	6.313	0.999

(b) Infusion Data

52.00	116.00	5.710	16.212	8.944	7.267	0.965
51.00	114.00	6.070	14.987	8.282	6.705	0.950
55.00	120.00	3.520	27.205	14.736	12.469	0.974
45.00	106.00	2.860	29.576	17.020	12.556	0.973
46.00	108.00	2.160	39.900	22.906	16.994	1.000
59.00	124.00	2.010	49.230	25.806	23.424	0.982
43.00	104.00	0.900	92.213	54.087	38.127	1.000

TABLE RE-19 (cont.)

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
55.00	120.00	1.990	48.121	26.065	22.055	0.877
45.00	106.00	0.970	87.204	50.184	37.021	1.000
43.00	104.00	0.990	83.830	49.170	34.661	1.000

ADRENALINE INFUSION NO. 2

(a) Pre-Infusion Data

33.00	88.00	5.460	12.862	8.038	4.823	0.998
30.00	82.00	3.270	20.011	12.690	7.321	0.975
31.00	85.00	2.900	23.390	14.859	8.530	0.993
28.00	78.00	2.360	26.375	16.907	9.468	1.000
38.00	96.00	3.850	19.898	12.022	7.876	0.952
29.00	80.00	2.410	26.490	16.887	9.602	0.959
31.00	84.00	2.150	31.178	19.672	11.506	0.983
24.00	56.00	1.900	23.520	13.440	10.080	0.984
24.00	58.00	1.410	32.826	19.243	13.583	1.000

(b) Infusion Data

31.00	84.00	4.180	16.036	10.118	5.918	0.999
33.00	88.00	2.340	30.010	18.756	11.254	0.983
29.00	80.00	1.350	47.289	30.147	17.142	0.970
24.00	48.00	1.040	36.831	18.415	18.415	1.000
24.00	50.00	1.380	28.913	15.035	13.878	0.973

TABLE RE-20

EXPERIMENT NO. RE-20

ADRENALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
40.00	134.00	12.040	8.881	6.230	2.651	0.999
43.00	144.00	13.550	8.481	5.948	2.532	0.994
48.00	146.00	15.760	7.393	4.962	2.430	0.998
45.00	144.00	15.850	7.250	4.984	2.266	0.998
48.00	154.00	18.500	6.643	4.572	2.070	0.993
45.00	144.00	16.210	7.089	4.874	2.215	1.000
45.00	142.00	16.100	7.038	4.808	2.230	0.989
45.00	148.00	16.490	7.162	4.984	2.178	0.998
45.00	112.00	16.310	5.480	3.278	2.202	1.000
33.00	112.00	14.690	6.084	4.291	1.793	0.994

(b) Infusion Data

33.00	114.00	13.700	6.640	4.718	1.922	0.997
35.00	124.00	15.670	6.315	4.532	1.782	0.994
37.00	132.00	18.040	5.839	4.202	1.637	0.997
37.00	156.00	18.950	6.569	5.011	1.558	0.997
45.00	168.00	23.800	5.633	4.124	1.509	0.996
48.00	168.00	27.810	4.821	3.443	1.377	1.000
48.00	168.00	27.030	4.960	3.543	1.417	0.998
48.00	166.00	26.140	5.068	3.602	1.465	0.994
45.00	160.00	28.580	4.467	3.211	1.256	1.000
45.00	160.00	26.700	4.782	3.437	1.345	0.998

TABLE RE-21

EXPERIMENT NO. RE-21

ADRENALINE INFUSION NO. 1

(a) Pre-Infusion Data

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
18.00	114.00	3.230	28.165	23.718	4.447	0.990
17.00	108.00	2.270	37.967	31.990	5.976	0.956
17.00	109.00	3.070	28.333	23.914	4.419	0.994
17.00	108.00	2.790	30.890	26.028	4.862	0.991
16.00	103.00	2.220	37.024	31.273	5.751	1.000
17.00	110.00	2.890	30.374	25.680	4.694	0.991
16.00	100.00	2.260	35.310	29.660	5.560	1.000
16.00	102.00	2.250	36.176	30.501	5.675	1.000
16.00	104.00	2.360	35.166	29.756	5.410	1.000
17.00	106.00	2.420	34.954	29.348	5.606	1.000
16.00	104.00	2.360	35.166	29.756	5.410	1.000
16.00	100.00	68.850	1.159	0.974	0.185	0.617

(b) Infusion Data

15.00	96.00	2.580	29.693	25.053	4.640	0.991
16.00	104.00	2.360	35.166	29.756	5.410	1.000
16.00	100.00	2.260	35.310	29.660	5.650	1.000
18.00	116.00	2.570	36.019	30.430	5.589	1.000
18.00	116.00	2.760	33.539	28.335	5.204	0.991
18.00	118.00	3.050	30.873	26.164	4.710	0.994
20.00	127.00	3.210	31.572	26.600	4.972	0.970

TABLE RE-21 (cont.)

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
19.00	123.00	3.270	30.017	25.380	4.637	0.994
20.00	128.00	3.170	32.222	27.187	5.035	0.970
20.00	126.00	3.690	27.249	22.924	4.325	0.982
19.00	123.00	4.390	22.359	18.905	3.454	0.986
19.00	120.00	3.760	25.468	21.436	4.032	1.000

ADRENALINE INFUSION NO. 2

(a) Pre-Infusion Data

14.00	92.00	2.240	32.775	27.787	4.987	1.000
15.00	96.00	2.150	35.632	30.064	5.567	0.876
14.00	92.00	2.210	33.220	28.165	5.055	1.000
14.00	94.00	2.390	31.386	26.711	4.674	1.000
16.00	100.00	2.380	33.529	28.165	5.365	1.000
16.00	100.00	2.310	34.545	29.018	5.527	1.000
16.00	100.00	2.060	38.738	32.540	6.198	0.982
15.00	98.00	2.450	31.920	27.034	4.886	1.000

(b) Infusion Data

13.00	86.00	5.010	13.698	11.628	2.071	0.929
13.00	86.00	4.700	14.602	12.394	2.207	0.988
14.00	94.00	8.790	8.534	7.263	1.271	0.983
14.00	90.00	7.570	9.487	8.012	1.494	0.971
14.00	92.00	7.480	9.815	8.321	1.494	0.979
13.00	88.00	8.310	8.451	7.202	1.248	0.989

TABLE RE-21 (cont.)

P.C.P.	A.B.P.	FLOW	C.R.	C.V.R.	P.C.R.	C.C. ²
14.00	90.00	7.570	9.487	8.012	1.476	0.971
15.00	96.00	8.980	8.531	7.198	1.333	0.989

2. EXPERIMENTAL DATA REFERRING TO
EXPONENTIAL NATURE OF DIE AWAY CURVES

A. Die Away Curves Using Manometric Perfusion Apparatus On
A Live Dog

(see also Appendix I, Fig. AI-1a to AI-6a)

Figures AI-7a to AI-30a which follow, together with
Figures AI-1a to AI-6a (see Appendix I) are curves from
which the data in Appendix I, Figures AI-1b and AI-30b and
Table AI-1 are derived.

B. Natural Logarithms of Die Away Curves Using Manometric
Perfusion Apparatus and Natural Logarithms of (Die Away
Curves Minus Peripheral Coronary Pressures)

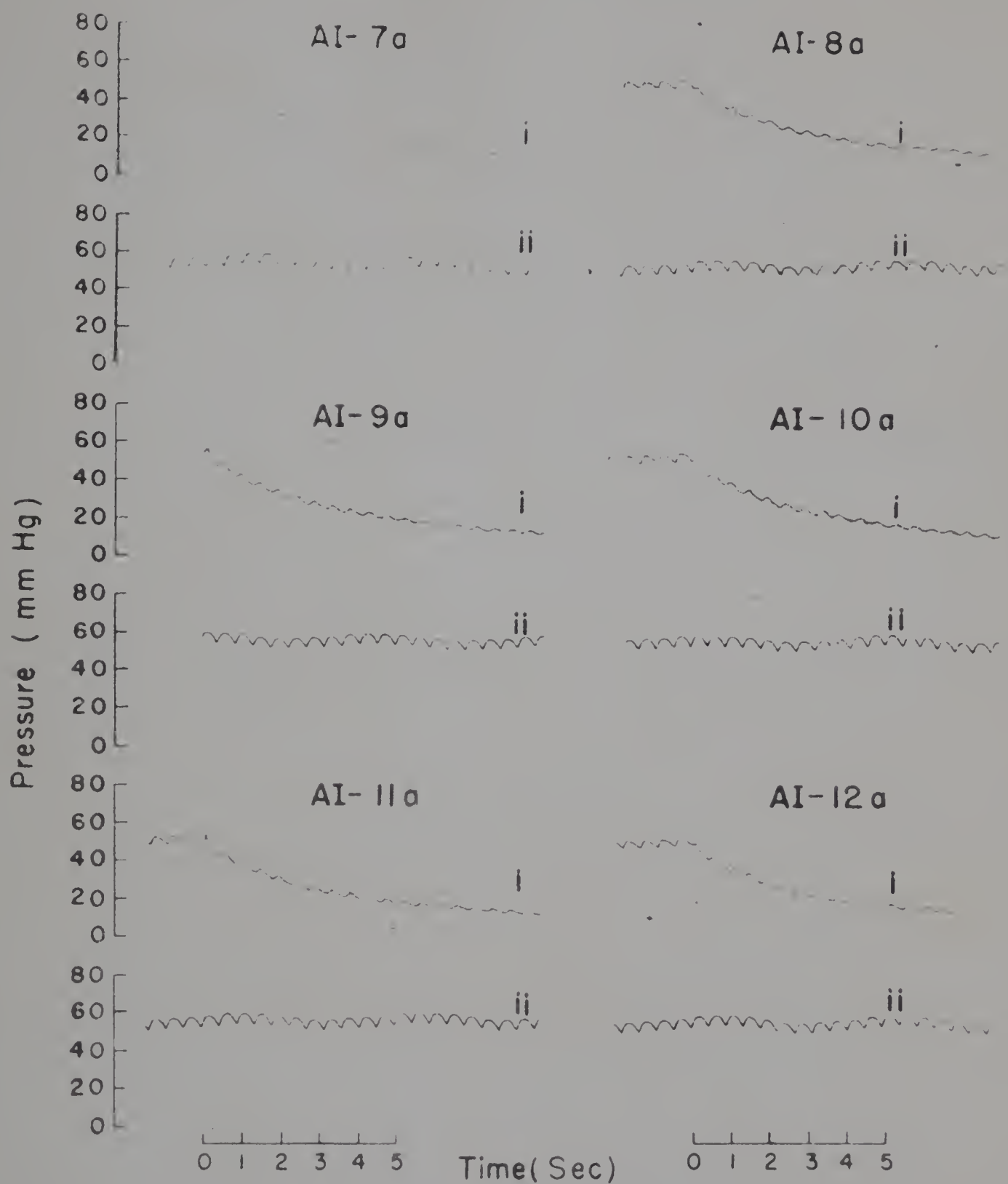
(see also Appendix I, Fig. AI-1b to AI-8b)

Figures AI-9b to AI-30b which follow, together with
Figures AI-1b to AI-8b (see Appendix I) are curves anala-
gous to those in AI-1a to AI-30a but with logarithms taken
of the pressures before and after subtracting peripheral
coronary pressures.

FIGURES AI-7a TO AI-30a

ACTUAL PRESSURE 'DIE-AWAYS'
FROM MANOMETRIC PERFUSION
APPARATUS ON A LIVE DOG

Figures AI- 7a - AI- 12a

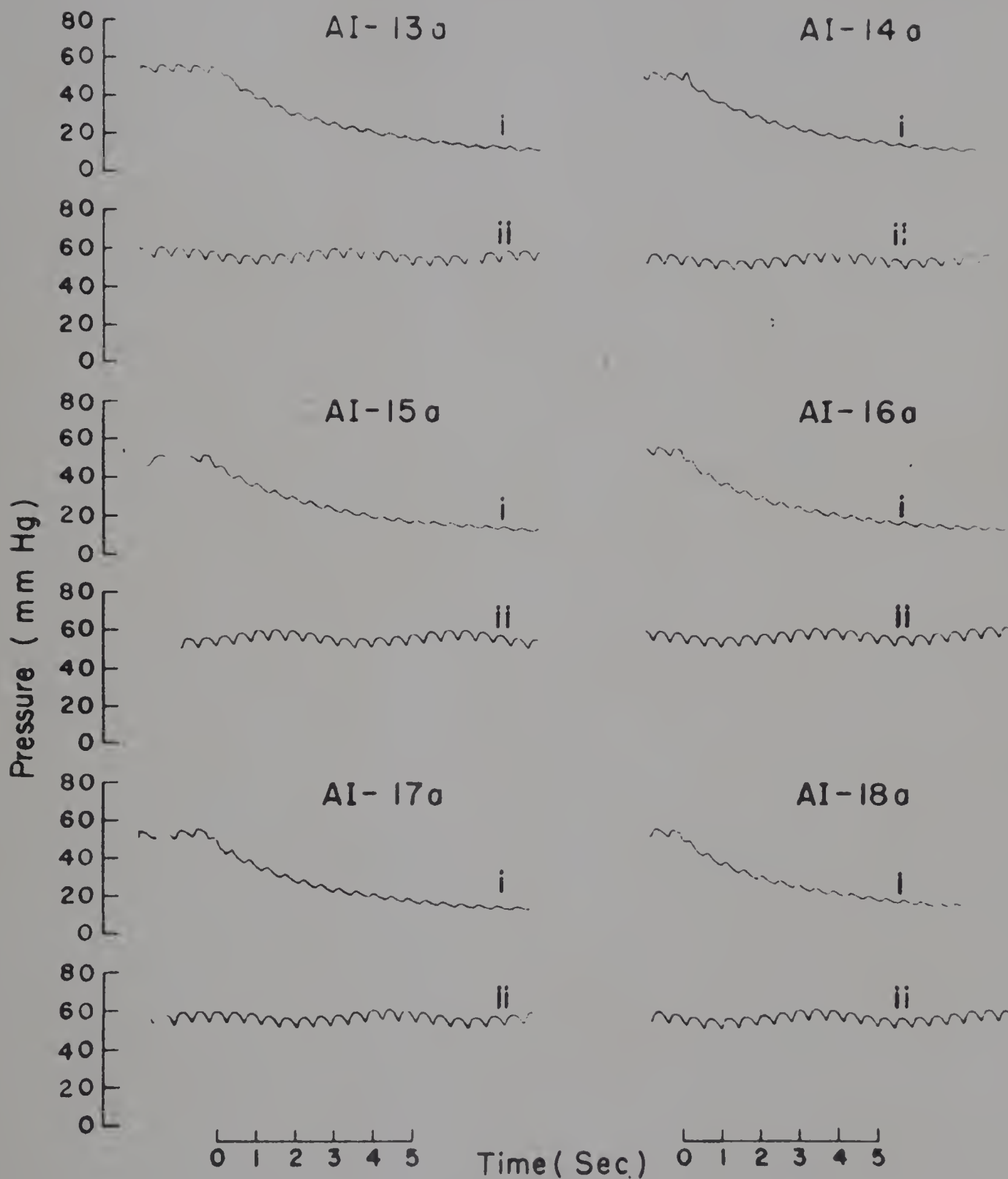


i Actual Pressure "Die-Aways" from Manometric Perfusion Apparatus on a Live Dog

ii Aortic Blood Pressure

For full explanation see text, pp. 120, paragraph 2.

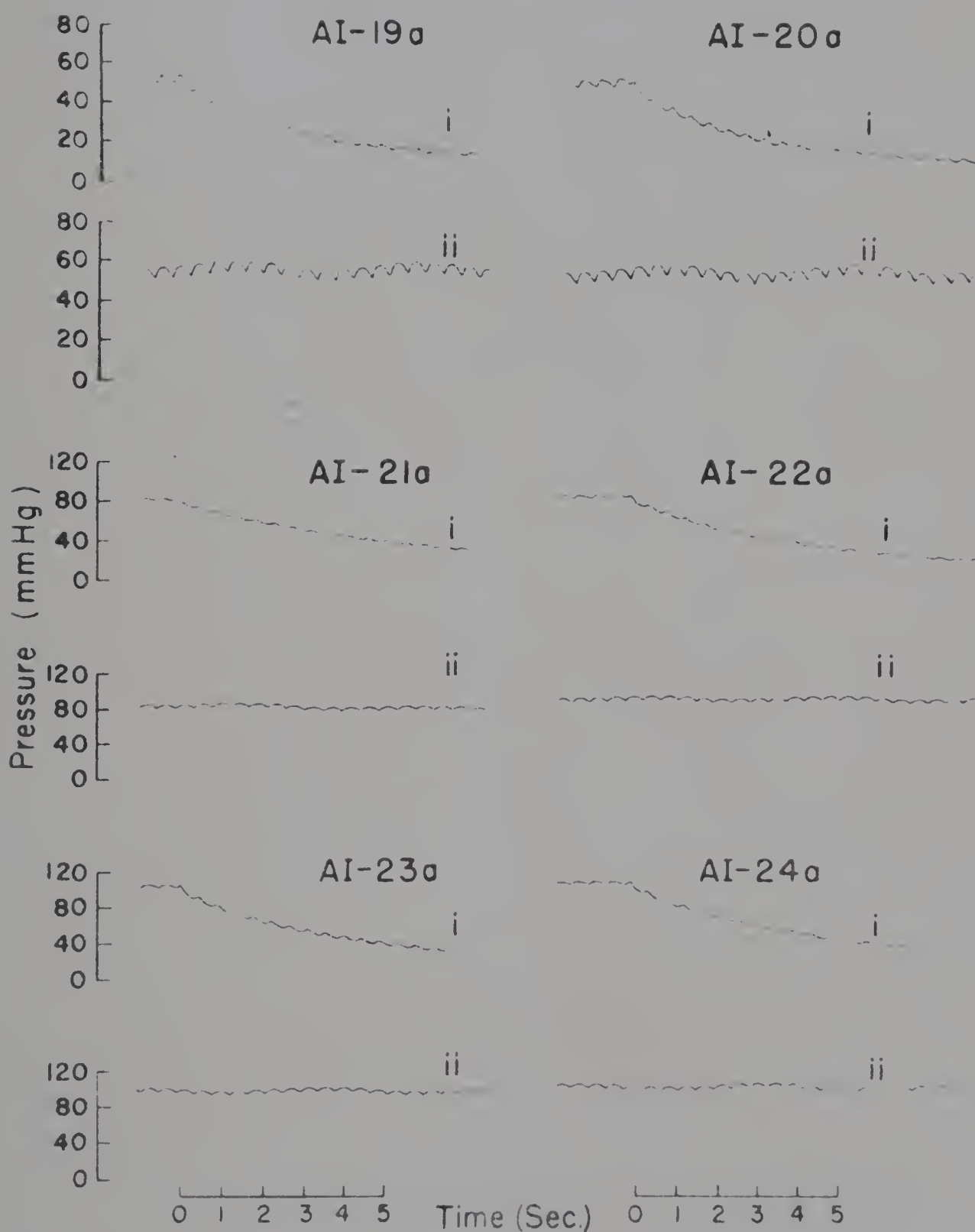
Figures AI-13a - AI-18a



i Actual Pressure "Die-Aways" from Manometric
Perfusion Apparatus on a Live Dog
ii Aortic Blood Pressure

For full explanation see text, pp. 120, paragraph 2.

Figures AI-19a- AI-24a

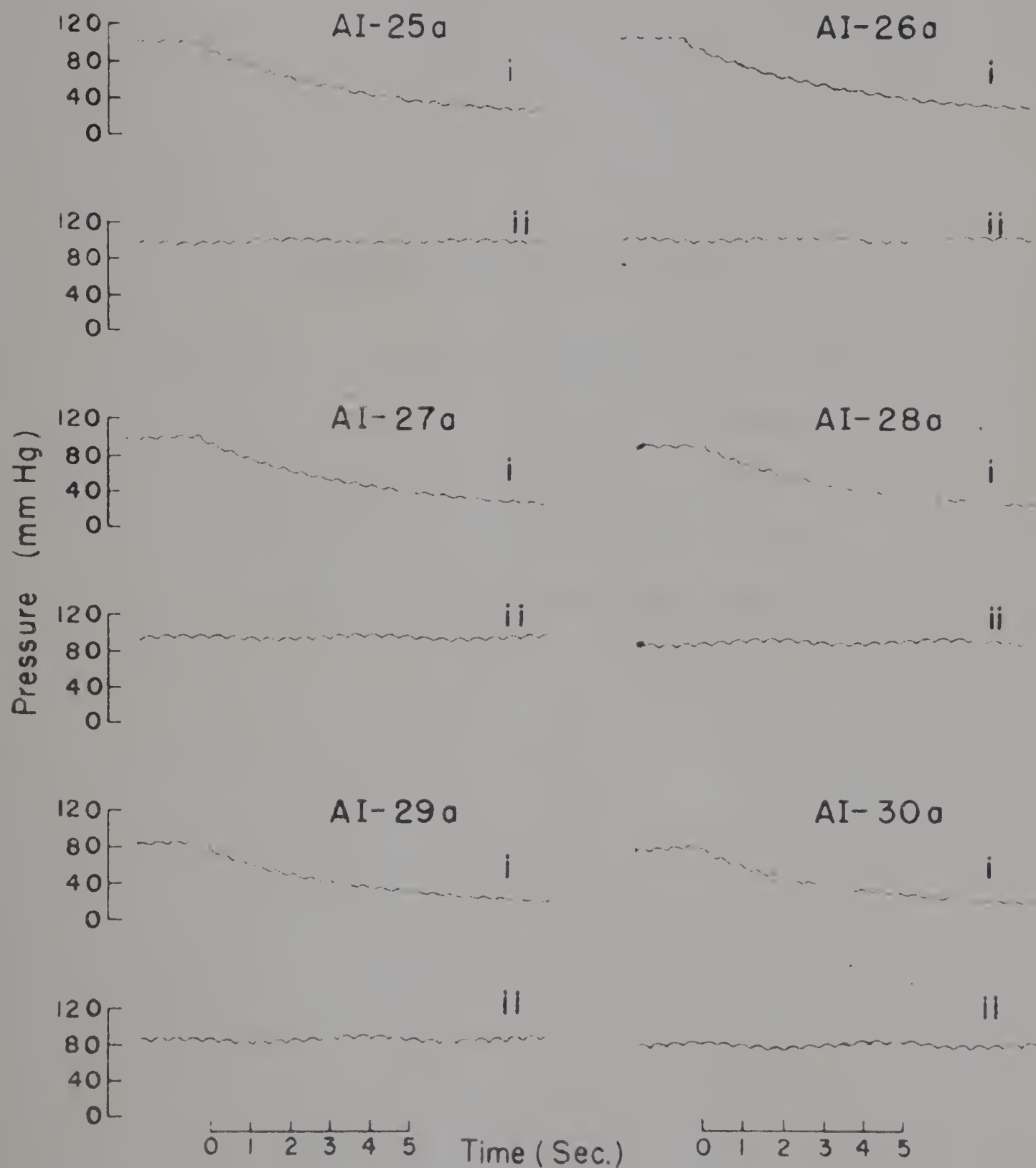


i Actual Pressure "Die-Aways" from Manometric Perfusion Apparatus on a Live Dog

ii Aortic Blood Pressure

For full explanation see text, pp. 120, paragraph 2.

Figures AI-25a AI-30a



i Actual Pressure "Die-Aways" from Manometric
Perfusion Apparatus on a Live Dog

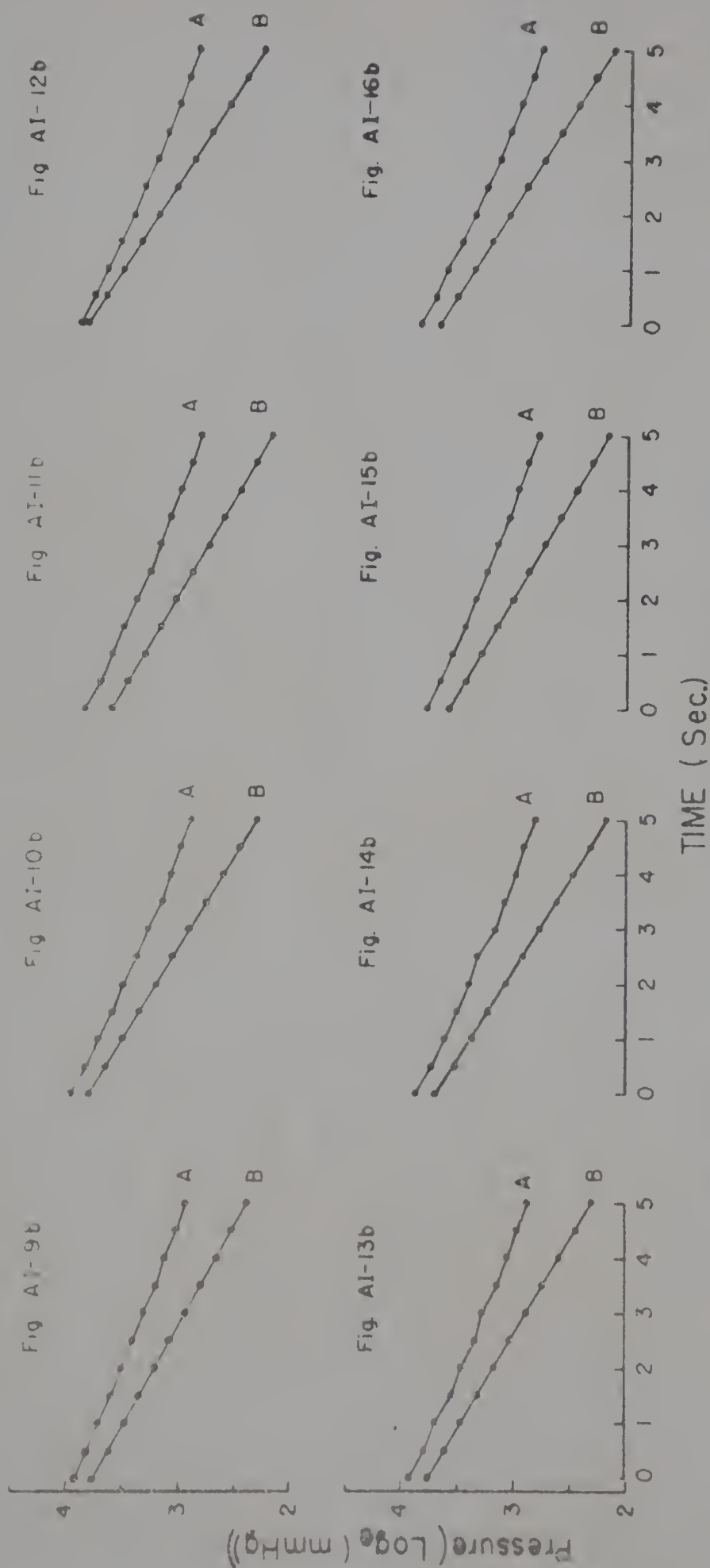
ii Aortic Blood Pressure

For full explanation see text, pp. 120, paragraph 2.

FIGURES AI-9b TO AI-30b

NATURAL LOGARITHMS OF PRESSURE DIE-AWAYS
FROM MANOMETRIC PERFUSION APPARATUS
ON A LIVE DOG BEFORE (A CURVES)
AND AFTER (B CURVES) SUBTRACTING
PERIPHERAL CORONARY PRESSURES

FIGURES AI-9b- AI-16b

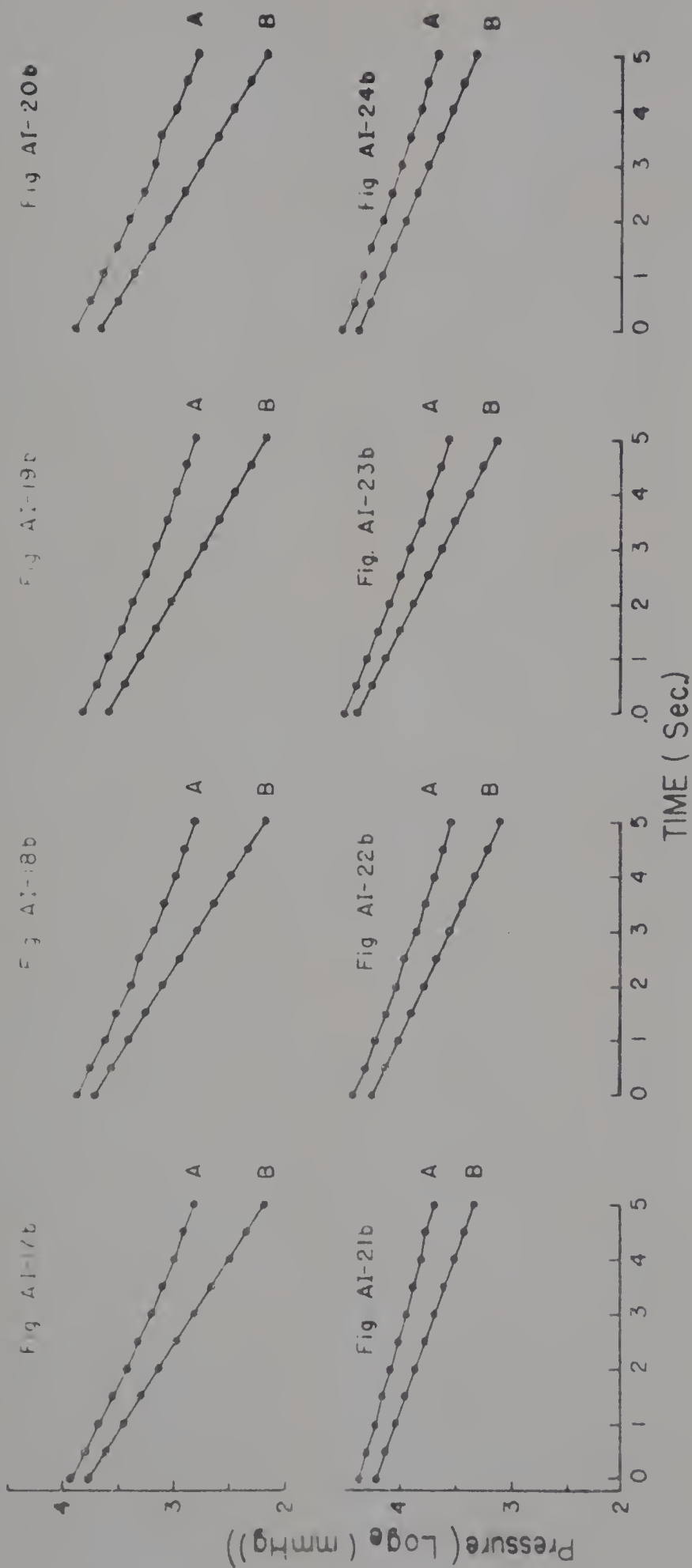


Pressure "Die-Aways" From Manometric Perfusion Apparatus

- A. Pressure($\text{Log}_e(\text{mmHg})$) vrs time
- B. Pressure minus P.C.P.($\text{Log}_e(\text{mmHg})$) vrs.time

For full explanation see text, pp. 120, paragraph 2.

FIGURES AI-17b; AI-24b

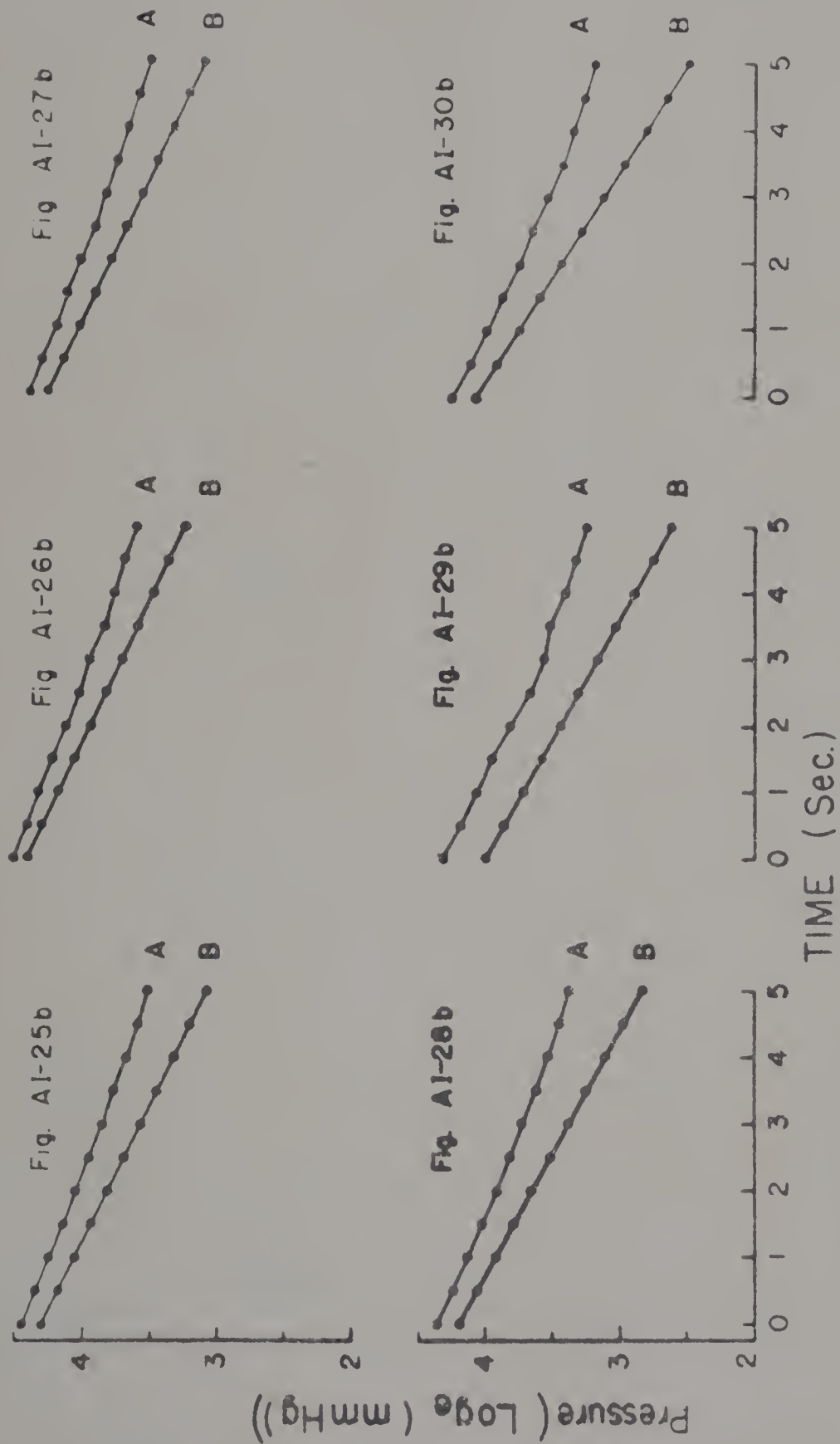


Pressure "Die-Aways" From Manometric Perfusion Apparatus

- A Pressure(Log_e(mmHg)) vrs. time
- B. Pressure minus PC.P (Log_e(mmHg)) vrs time

For full explanation see text, pp. 120, paragraph 2.

FIGURES AI-25b - AI-30b



Pressure "Die-Aways" From Manometric Perfusion Apparatus

A. Pressure($\text{Log}_e(\text{mm Hg})$) vrs time

B. Pressure minus PC.P ($\text{Log}_e(\text{mmHg})$) vrs.time

For full explanation see text, pp. 120, paragraph 2.

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